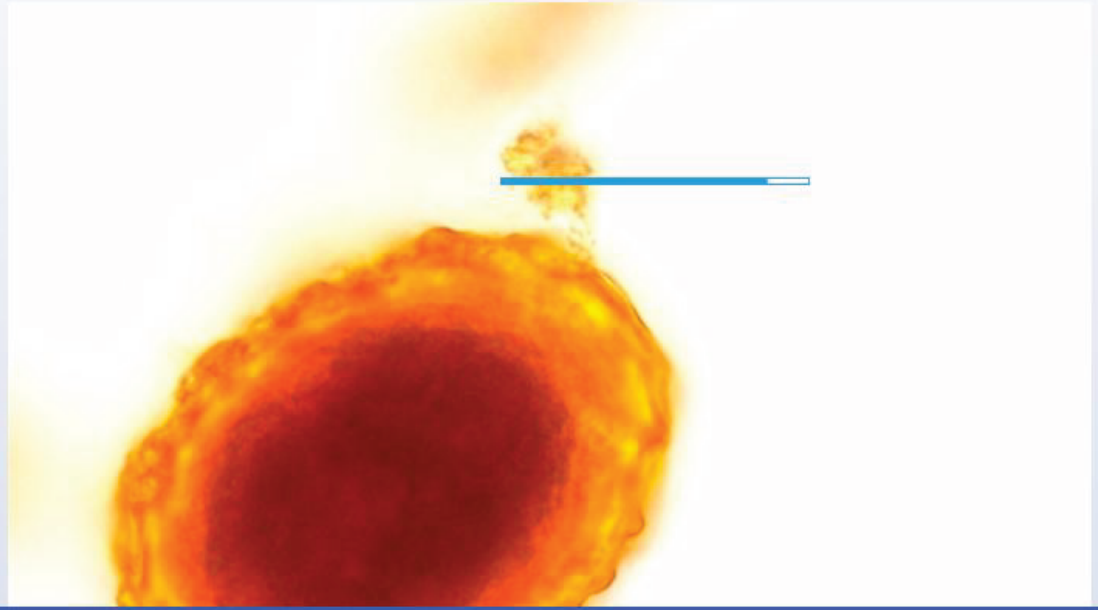
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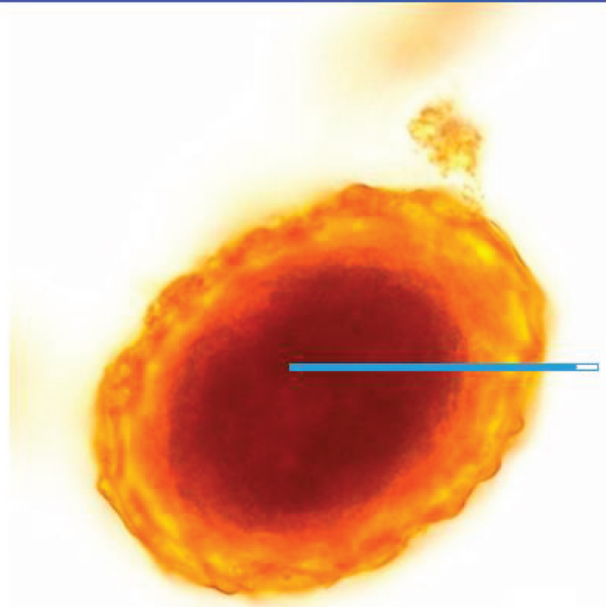
A 16-year-old previously healthy adolescent developed nonproductive cough, dyspnea, and wheezing after traveling abroad. The patient has no history of allergies and has had no recent upper respiratory illness. The symptoms spontaneously resolved after several days, but soon after, she began having abdominal discomfort, anorexia, and nausea. Stool microscopy results are shown in the following image:



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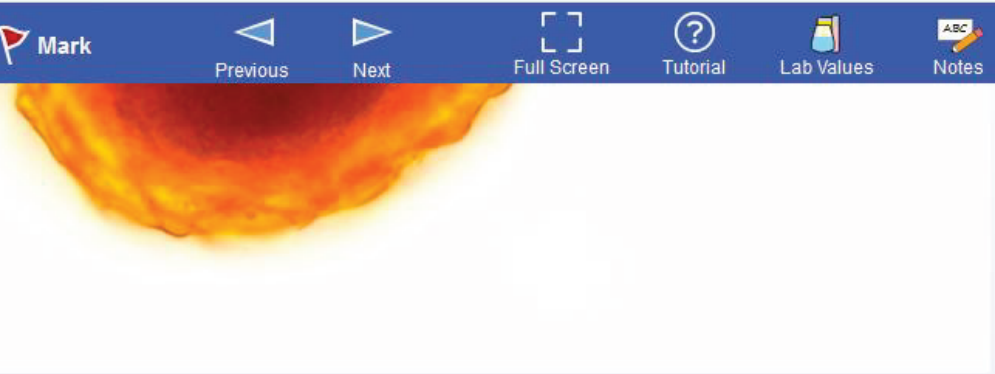
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Which of the following was the most likely cause of this patient's pulmonary symptoms?

A. Formation of cross-reacting antibodies (2%)

B. Immune response against inhaled spores (7%)

C. Parasite-induced cardiac dysfunction (1%)

D. Transpulmonary migration of larvae (84%)

E. Type IV hypersensitivity to a foreign antigen (2%)

Correct

84%

41 secs

01/14/2021

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This patient's recent travel, transient pulmonary symptoms, and subsequent gastrointestinal manifestations are suspicious for a **parasitic infection** involving the lungs and intestines. Stool microscopy reveals an oval egg with a thick outer shell and a single interior ovum, thereby confirming ***Ascaris lumbricoides*** (roundworm) infection.

A lumbricoides is a common parasitic infection in Asia, Africa, and South America. Most cases in the United States arise in **travelers** to these regions. Transmission occurs when **eggs are ingested** via contaminated food or water. Eggs hatch into larvae in the small intestine, penetrate the intestinal wall, and **migrate to the alveoli**, where they mature. Pulmonary infection is generally asymptomatic, but a minority of infected individuals develop **Loeffler syndrome**, a transient, **eosinophilic pneumonitis** with pulmonary symptoms (eg, dry cough, dyspnea, wheezing).

After several days, larvae are coughed out of the alveoli and subsequently swallowed into the gastrointestinal tract, where they mature into long (25- to 35-cm) adult worms that shed up to 200,000 eggs per day. Most gastrointestinal infections are asymptomatic, but some patients have abdominal discomfort, nausea/vomiting, and diarrhea. The diagnosis of **gastrointestinal tract infection** is made by inspecting the stool for eggs; treatment with antiparasitic drugs (eg, albendazole) is generally curative.

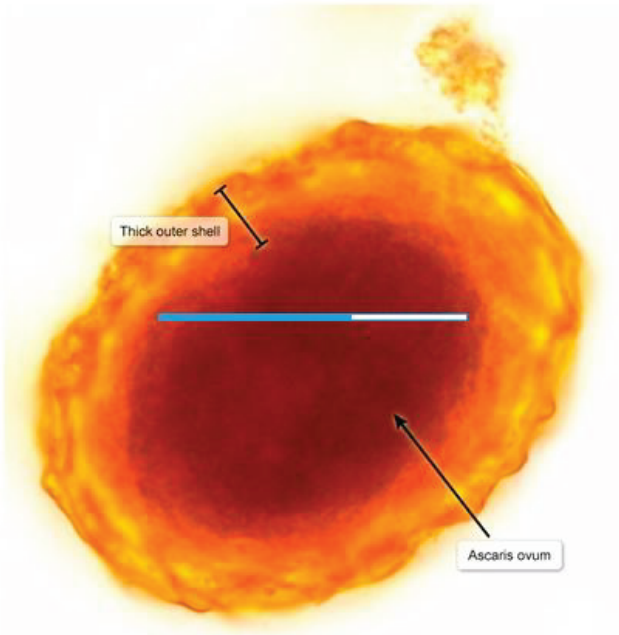
(Choice A) Rheumatic fever is associated with the formation of cross-reacting antibodies to renal,

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Ascaris lumbricoides



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(Choice A) Rheumatic fever is associated with the formation of cross-reacting antibodies to renal,

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Ascaris lumbricoides



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(Choice A) Rheumatic fever is associated with the formation of cross-reacting antibodies to renal, neuronal, and cardiac antigens following group A *Streptococcus* pharyngitis. Eggs would not be seen in stool.

(Choice B) Hypersensitivity pneumonitis, an immune reaction to an inhaled agent, can occur following exposure to mold dust or spores. Patients generally develop acute fever, nausea, cough, and dyspnea. However, wheezing is uncommon, and eggs would not be shed in stool.

(Choice C) Chagas disease, a parasitic infection caused by *Trypanosoma cruzi*, can cause myopericarditis during acute infection. However, cardiac and gastrointestinal manifestations are much more likely to occur years or decades later. In addition, *T cruzi* is not shed in stool; it can sometimes be visualized on blood smear.

(Choice E) Type IV hypersensitivity reactions are mediated by T cells and are often seen as part of certain drug reactions (eg, Stevens-Johnson syndrome). In contrast, *Ascaris* infections are associated with IgE-mediated (eosinophilic) hypersensitivity.

Educational objective:

Ascaris lumbricoides is transmitted via contaminated food or water. Eggs hatch into larvae in the small intestine, penetrate the intestinal wall, and migrate across the lung into the alveoli. Larvae are

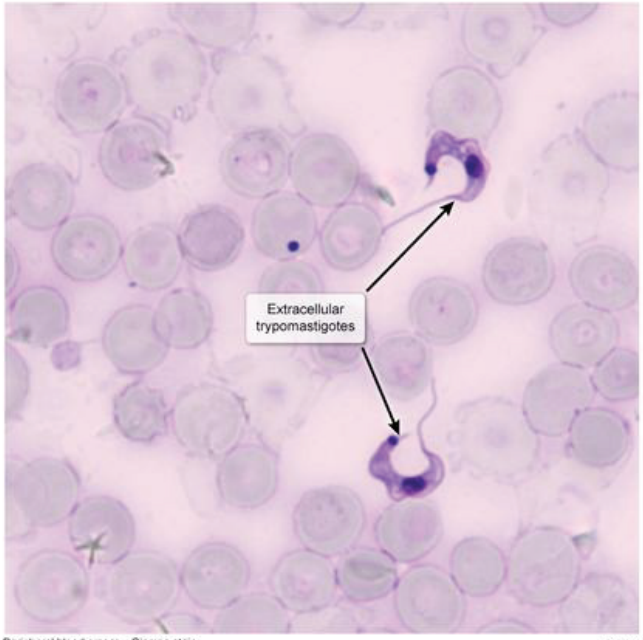
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(Choice A) Rheumatic fever is associated with the formation of cross-reacting antibodies to renal

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Trypanosoma cruzi



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(Choice C) Chagas disease, a parasitic infection caused by *Trypanosoma cruzi*, can cause myopericarditis during acute infection. However, cardiac and gastrointestinal manifestations are much more likely to occur years or decades later. In addition, *T cruzi* is not shed in stool; it can sometimes be visualized on blood smear.

(Choice E) Type IV hypersensitivity reactions are mediated by T cells and are often seen as part of certain drug reactions (eg, Stevens-Johnson syndrome). In contrast, *Ascaris* infections are associated with IgE-mediated (eosinophilic) hypersensitivity.

Educational objective:

Ascaris lumbricoides is transmitted via contaminated food or water. Eggs hatch into larvae in the small intestine, penetrate the intestinal wall, and migrate across the lung into the alveoli. Larvae are subsequently coughed up and swallowed into the gastrointestinal tract, where they mature to adult worms. Most patients are asymptomatic, but some develop early pulmonary manifestations (Loeffler syndrome) or later gastrointestinal symptoms.

Microbiology	Infectious Diseases	Intestinal helminth parasites
Subject	System	Topic

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A 56-year-old woman comes to the emergency department due to 1 day of fever. She has a history of a hematologic malignancy and recently completed a cycle of chemotherapy through an indwelling central venous catheter. Temperature is 38.3 C (100.9 F). Laboratory studies are notable for neutropenia, with an absolute neutrophil count of 380/mm^3. The patient is started on broad-spectrum antibiotics. Three days later, she continues to be febrile. Fungal cultures grow a species of *Candida* with a mutation in a gene coding an enzyme responsible for synthesizing a fungal cell wall polysaccharide. The organism is most likely to be resistant to which of the following antifungal agents as a result of this mutation?

- A. Amphotericin B
- B. Caspofungin
- C. Flucytosine
- D. Griseofulvin
- E. Itraconazole
- F. Terbinafine

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hematologic malignancy and recently completed a cycle of chemotherapy through an indwelling central venous catheter. Temperature is 38.3 C (100.9 F). Laboratory studies are notable for neutropenia, with an absolute neutrophil count of 380/mm^3. The patient is started on broad-spectrum antibiotics. Three days later, she continues to be febrile. Fungal cultures grow a species of *Candida* with a mutation in a gene coding an enzyme responsible for synthesizing a fungal cell wall polysaccharide. The organism is most likely to be resistant to which of the following antifungal agents as a result of this mutation?

A. Amphotericin B (20%)
✓ B. Caspofungin (46%)
C. Flucytosine (2%)
D. Griseofulvin (3%)
E. Itraconazole (23%)
F. Terbinafine (4%)

Correct

46%
35 secs
11/15/2020

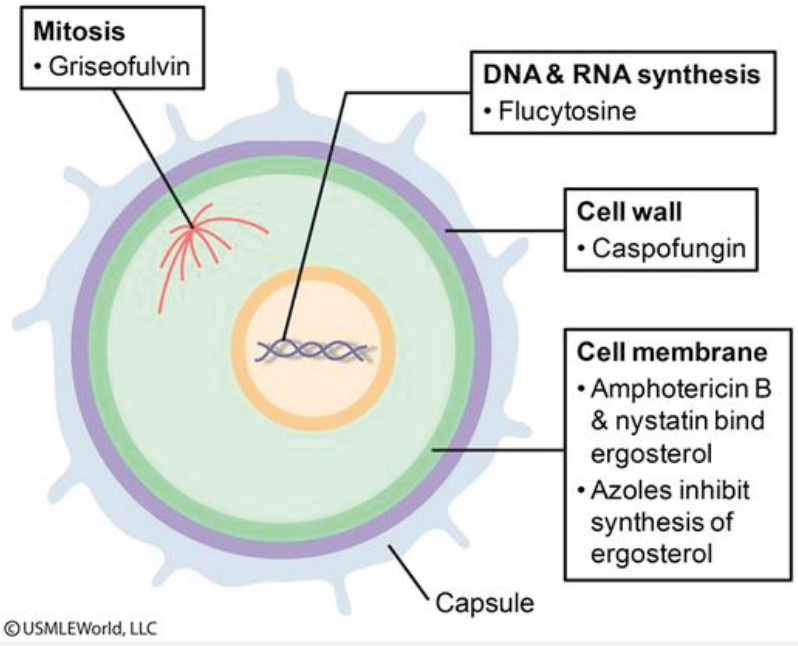
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46%
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Antifungal targets



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A major polysaccharide component of the fungal cell wall is **1,3-beta-D-glucan**. **Caspofungin** and the other **echinocandin** antifungals (eg, micafungin) block **glucan** synthesis. Whereas polyene and azole antifungals target the fungal cell membrane, the echinocandins are unique in that they suppress fungal **cell wall** synthesis. Caspofungin is most active against *Candida* species and *Aspergillus.* It is not active against *Cryptococcus neoformans* and has limited activity against *Mucor* and *Rhizopus* species. This patient likely has an infection due to a caspofungin-resistant strain of *Candida* (uncommon).

(Choice A) Amphotericin B is a polyene antifungal that binds ergosterol in the fungal cell membrane and leads to pore formation and cell lysis.

(Choice C) Flucytosine inhibits the synthesis of both DNA (replication) and RNA (protein synthesis) in fungal cells. It is mainly used as a synergistic agent with amphotericin B, particularly in the treatment of cryptococcal meningitis.

(Choice D) Griseofulvin enters fungal cells, binds microtubules, and inhibits mitosis. This antifungal drug is effective only against dermatophyte fungi as it accumulates in keratin-containing tissues.

(Choice E) Itraconazole is an azole antifungal that inhibits ergosterol synthesis. It does not affect the polysaccharides of the fungal cell wall.

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fungal cells. It is mainly used as a synergistic agent with amphotericin B, particularly in the treatment of cryptococcal meningitis.

(Choice D) Griseofulvin enters fungal cells, binds microtubules, and inhibits mitosis. This antifungal drug is effective only against dermatophyte fungi as it accumulates in keratin-containing tissues.

(Choice E) Itraconazole is an azole antifungal that inhibits ergosterol synthesis. It does not affect the polysaccharides of the fungal cell wall.

(Choice F) Terbinafine accumulates in skin and nails and is used to treat dermatophytosis. Terbinafine inhibits the fungal enzyme squalene epoxidase, which ultimately results in decreased ergosterol synthesis.

Educational objective:
Echinocandins (eg, caspofungin, micafungin) are antifungal medications that inhibit synthesis of the polysaccharide glucan, an essential component of the fungal cell wall.

Microbiology	Infectious Diseases	Antibiotic resistance
Subject	System	Topic

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A previously healthy 27-year-old man comes to the clinic due to fever and rash. The patient is a missionary who recently immigrated from South Africa with his wife and 3 young children. Four days ago, he developed a high fever and malaise followed by the appearance of multiple discrete macules on his face, trunk, and extremities. The lesions are pruritic and evolved into pustules then vesicles. The patient has continued to develop new vesicles as other lesions crust over and heal. The remainder of the examination is unremarkable. This patient's symptoms are most likely due to an infection with which of the following pathogens?

- A. Coxsackievirus
- B. Herpes simplex virus
- C. Human herpesvirus 6
- D. Parvovirus
- E. Varicella-zoster virus
- F. Variola virus

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who recently immigrated from South Africa with his wife and 3 young children. Four days ago, he developed a high fever and malaise followed by the appearance of multiple discrete macules on his face, trunk, and extremities. The lesions are pruritic and evolved into pustules then vesicles. The patient has continued to develop new vesicles as other lesions crust over and heal. The remainder of the examination is unremarkable. This patient's symptoms are most likely due to an infection with which of the following pathogens?

A. ~~Coxsackievirus~~ (3%)
B. ~~Herpes simplex virus~~ (3%)
C. Human herpesvirus 6 (6%)
D. ~~Parvovirus~~ (1%)
E. Varicella-zoster virus (78%)
F. Variola virus (7%)

Correct

78%

01 min, 22 secs

02/07/2021

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Primary varicella	
Epidemiology	• Primary infection (ie, chickenpox) with varicella-zoster virus • Transmission via direct contact or aerosol droplets
Clinical features	• Prodrome (eg, fever, malaise) • Pruritic maculopapular rash followed by successive crops of vesicles in different stages • Mild in children, more severe in adolescents/adults
Management	• Prevention: varicella-zoster virus vaccine • Supportive care (eg, antihistamines) • Antiviral therapy (eg, acyclovir) in adults/immunocompromised

This patient has classic symptoms of **primary varicella-zoster virus** (VZV) infection, a vaccine-preventable illness that causes varicella, or **chickenpox**. Primary infection usually occurs in children but can develop at any age, with severe illness occurring more often in adolescents and adults.

Transmission of VZV occurs via aerosolized droplets or direct contact, and a **prodrome** of fever, headache, and malaise typically develops after a 2-week incubation period. Within a day, a **pruritic**, maculopapular

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can develop at any age, with severe illness occurring more often in adolescents and adults.

Transmission of VZV occurs via aerosolized droplets or direct contact, and a **prodrome** of fever, headache, and malaise typically develops after a 2-week incubation period. Within a day, a **pruritic**, maculopapular rash develops and evolves into pustules then vesicles. A characteristic finding in varicella is the development of **successive crops of lesions** on the face, trunk, and extremities, as seen in this patient with lesions in **different stages** of development (eg, crusted lesions, new vesicles). Vesicles crust over and resolve within 1-2 weeks. Once the primary infection has resolved, patients are at risk for reactivated infection (ie, herpes zoster).

(Choice A) Hand-foot-and-mouth disease, caused by coxsackievirus, presents with oral ulcers and a nonpruritic rash of variable morphology (eg, macular, vesicular) on the hands and feet. This patient's pruritus and lack of oral involvement make this diagnosis less likely.

(Choice B) Herpes simplex virus (HSV) in adults typically causes severe pharyngitis (primary infection) or a localized cluster of perioral vesicles (reactivated infection). Although HSV can cause a disseminated vesicular rash, this typically occurs in immunocompromised patients (eg, HIV). In addition, the rash is painful with vesicles in the same stage of development.

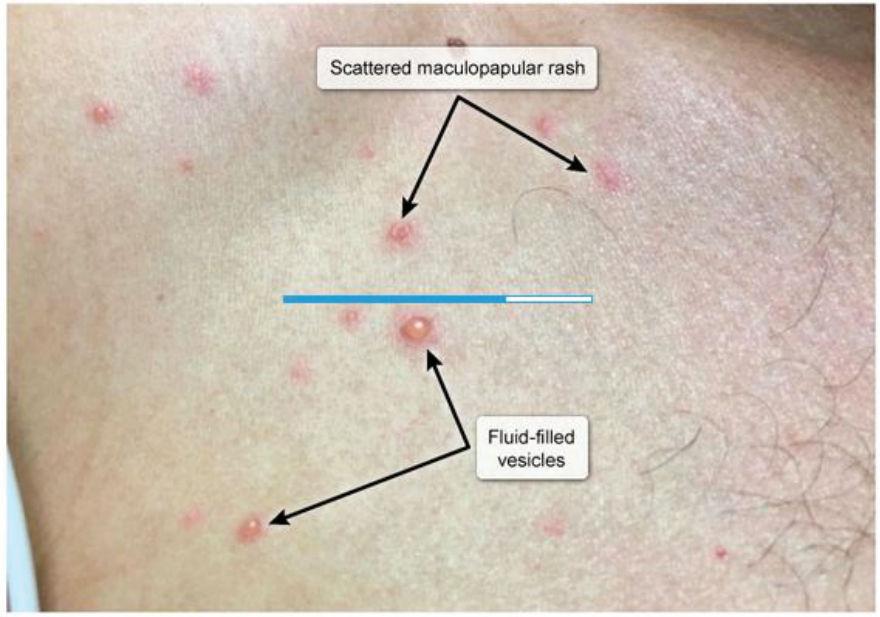
(Choice C) Human herpesvirus 6, which causes roseola infantum, most commonly presents with fever

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Varicella

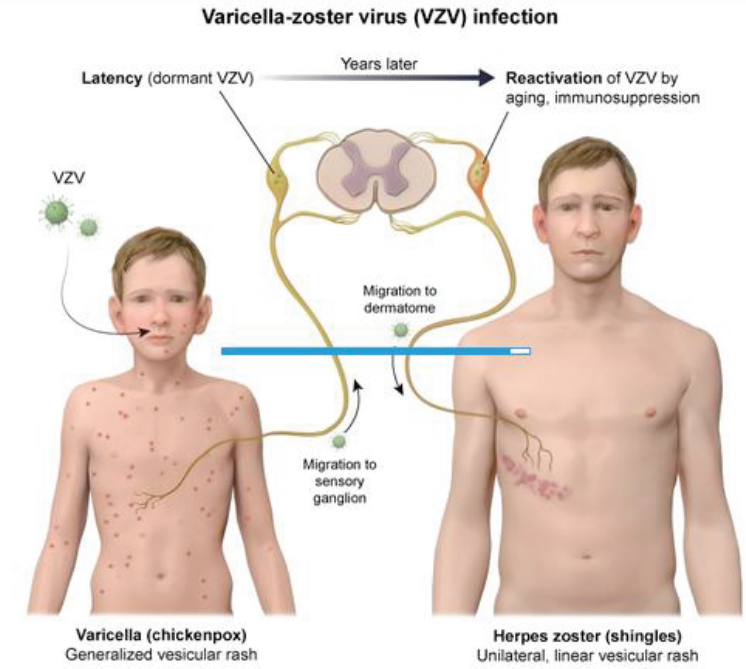


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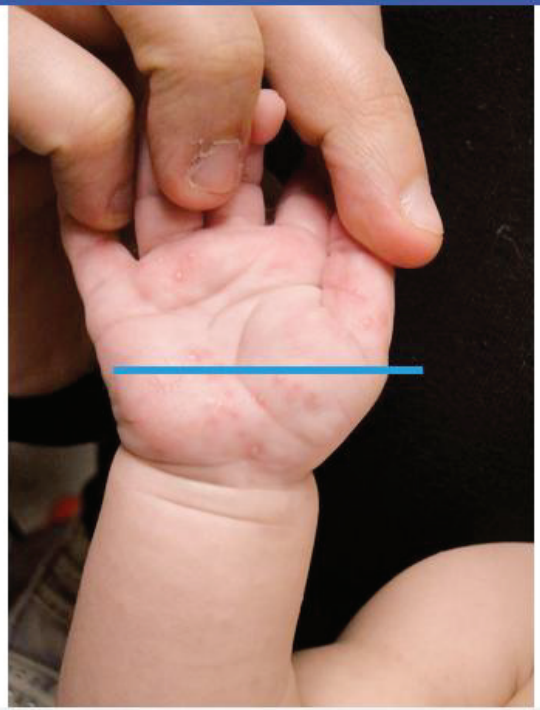


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vesicular rash, this typically occurs in immunocompromised patients (eg, HIV). In addition, the rash is painful with vesicles in the same stage of development.

(Choice C) Human herpesvirus 6, which causes roseola infantum, most commonly presents with fever followed by a diffuse, maculopapular rash in young children. Vesicles would not be seen, and infection in immunocompetent adults is rare.

(Choice D) Parvovirus causes erythema infectiosum. Prodromal symptoms (eg, fever, headache) are followed by the development of malar erythema (slapped-cheek rash) and a reticular truncal rash. This patient's vesiculopustular rash makes parvovirus unlikely.

(Choice F) Variola virus causes smallpox, which is characterized by a vesiculopustular rash with lesions at the same stage of development, unlike in this patient. Moreover, smallpox has been eradicated due to vaccination.

Educational objective:
Primary varicella zoster virus infection presents with a prodromal illness (eg, fever, malaise) followed by pruritic, vesicular lesions that appear in successive crops in different stages.

References

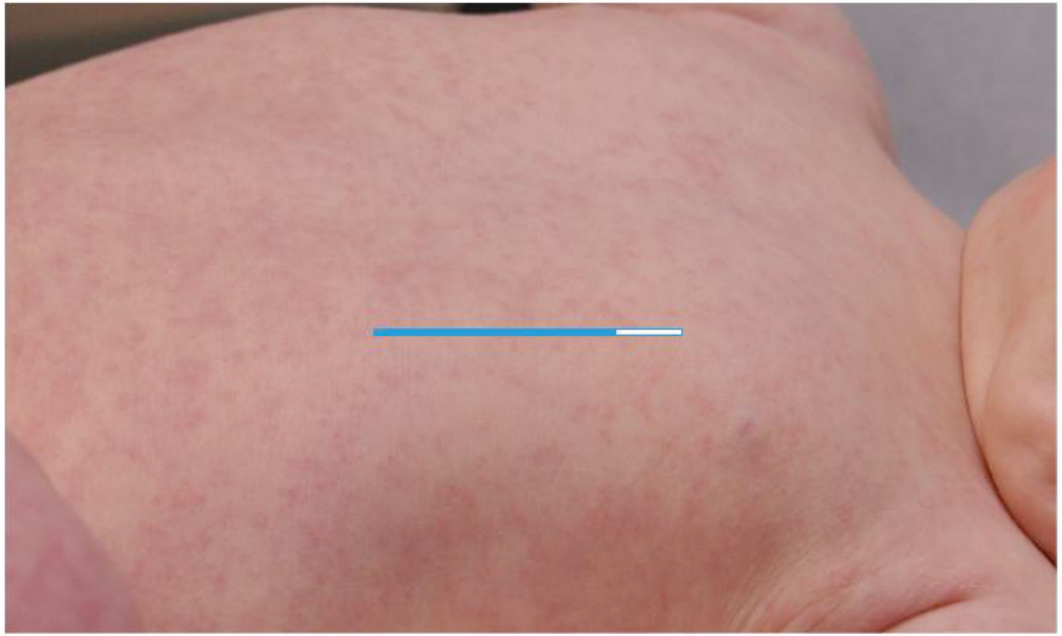
- Varicella zoster (chickenpox).

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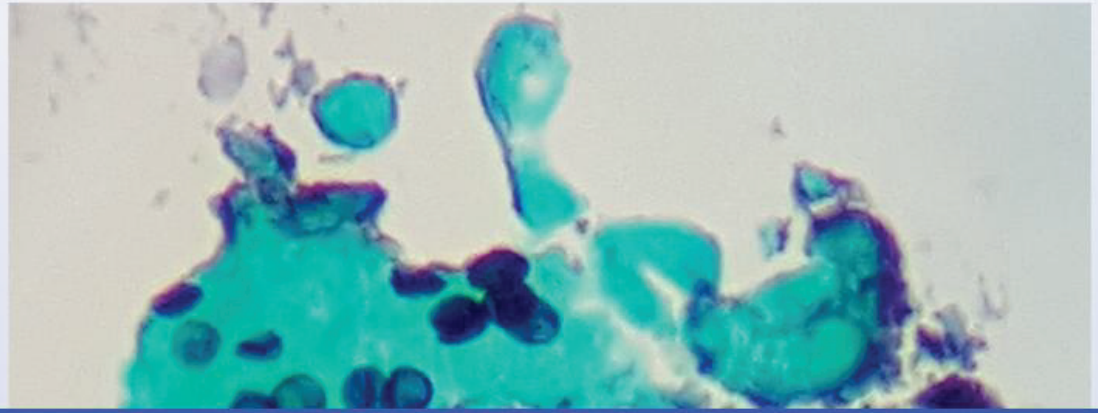


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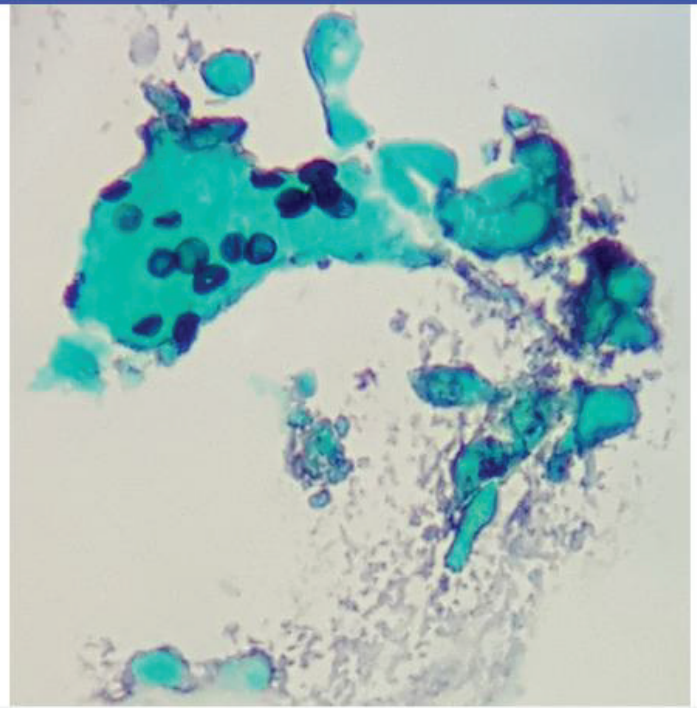
A 48-year-old homeless man is brought to the emergency department after being found unresponsive on the sidewalk. Medical history is unknown. Temperature is 38.3 C (101 F), blood pressure is 116/70 mm Hg, pulse is 108/min, and respirations are 26/min. Oxygen saturation is 88% on 100% oxygen via face mask. The patient is ill-appearing, thin, and disheveled with poor dentition. There are a few white patches on the oral mucosa, but no skin rash is present. Lung auscultation reveals bilateral crackles. There are healed abdominal scars from a previous surgery. The abdomen is soft with no hepatomegaly or splenomegaly. Chest x-ray reveals bilateral interstitial infiltrates. A silver-stained bronchoalveolar lavage specimen is shown in the image.



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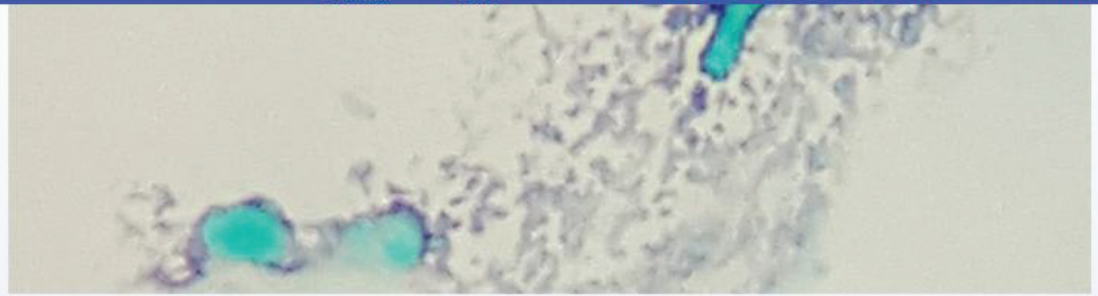
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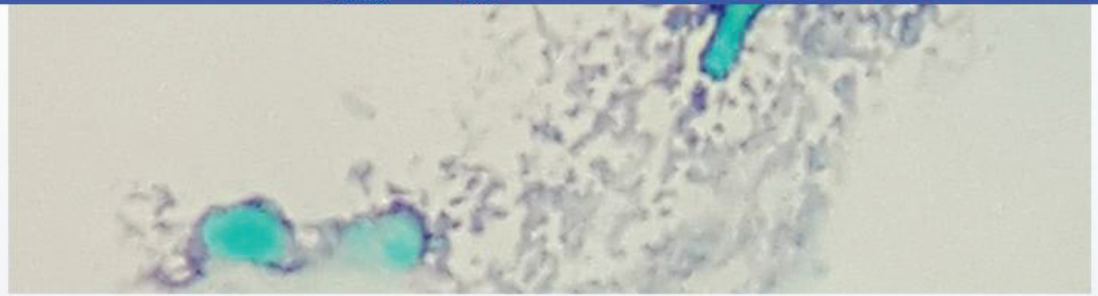


Which of the following most likely predisposed this patient to his current lung condition?

A. Aspiration of oropharyngeal secretion
B. Decreased mucociliary clearance
C. Defective antibody-specific response
D. Impaired cell-mediated immunity
E. Postsplenectomy state

Submit

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Which of the following most likely predisposed this patient to his current lung condition?

A. Aspiration of oropharyngeal secretion (16%)
B. Decreased mucociliary clearance (2%)
C. Defective antibody-specific response (3%)
D. Impaired cell-mediated immunity (71%)
E. Postsplenectomy state (6%)

Correct

71%

20 secs

02/21/2021

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This homeless patient has hypoxia, bilateral interstitial infiltrates, and a positive silver stain indicating likely ***Pneumocystis* pneumonia** (PCP), an atypical fungal infection caused by the opportunistic pathogen *P jirovecii*. Inhalation of the organism leads to inoculation of the **alveolar space**. Healthy individuals rarely develop symptoms as alveolar monocytes and macrophages are stimulated by the cell-mediated immune response to rapidly clear the organism. However, patients with **impaired cell-mediated immunity**, particularly those with untreated **AIDS** (CD4 count <200/mm^3), often cannot eliminate the pathogen.

PCP typically manifests with slowly worsening pulmonary symptoms (eg, cough, dyspnea), hypoxia, and chest x-ray evidence of a diffuse, bilateral interstitial infiltrate. Because *P jirovecii* cannot be cultured, diagnosis is made by identifying the organism in respiratory secretions using specialized stains (eg, methenamine silver stain).

This patient also has oral pharyngeal candidiasis (white patches on the oral mucosa), an opportunistic infection often seen in those with impaired cell-mediated immunity.

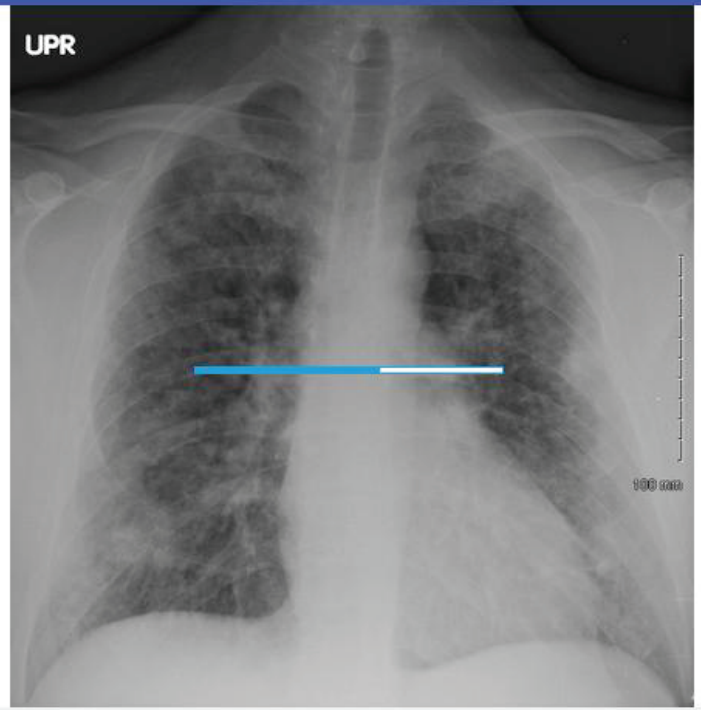
(Choice A) Aspiration pneumonia is common in patients who have impaired levels of consciousness. It usually presents with cough productive of foul-smelling sputum, dyspnea, fever, and a lobar infiltrate on chest x-ray. Most cases are caused by a mixture of anaerobic organisms.

(Choices B and E) Cigarette smoking impairs the ability of the cilia to clear mucus, which can lead to

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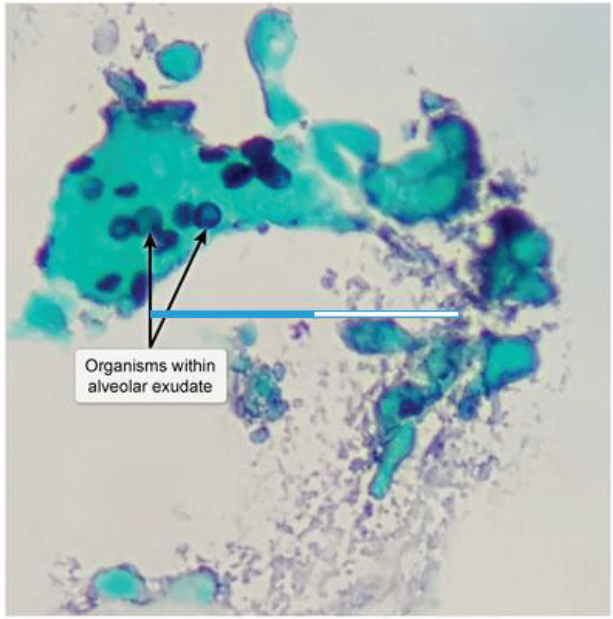
(Choices B and E) Cigarette smoking impairs the ability of the cilia to clear mucus, which can lead to

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***Pneumocystis jirovecii* pneumonia**



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Bronchoalveolar lavage – methenamine silver stain

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(Choices B and E) Cigarette smoking impairs the ability of the cilia to clear mucus, which can lead to

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usually presents with cough productive of foul-smelling sputum, dyspnea, fever, and a lobar infiltrate on chest x-ray. Most cases are caused by a mixture of anaerobic organisms.

(Choices B and E) Cigarette smoking impairs the ability of the cilia to clear mucus, which can lead to recurrent bacterial pneumonia. Patients with splenectomy are at increased risk for fulminant bacterial infections, particularly with encapsulated organisms such as *Streptococcus pneumoniae*. Bacterial pneumonia usually presents with cough productive of sputum, dyspnea, fever, and a lobar infiltrate on chest x-ray. The presence of diffuse interstitial infiltrates and a positive silver stain make PCP more likely.

(Choice C) The humoral antibody response is important for the elimination of pathogenic bacterial and viral infections. Although viral pneumonia can cause bilateral interstitial infiltrates, viruses are not identified on silver stain.

Educational objective:
Pneumocystis pneumonia is an atypical fungal infection seen primarily in those with impaired cell-mediated immunity (eg, advanced AIDS). Manifestations often include slowly worsening pulmonary symptoms, hypoxia, and bilateral interstitial infiltrates on chest x-ray. The cystic organism can be visualized using silver stain of respiratory secretions.

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A 52-year-old man comes to the emergency department due to several days of vague chest pain and cough. He immigrated to the United States from Taiwan 20 years ago. Temperature is 37.1 C (98.8 F). Physical examination reveals a decrescendo-type diastolic murmur over the right sternal border. Pulmonary auscultation reveals normal breath sounds with no wheezes or rales. Abdominal examination shows no organomegaly. Serum fluorescent treponemal antibody absorption testing is positive. Chest x-ray reveals mediastinal widening. The pathologic process most likely responsible for this patient's symptoms starts as which of the following?

A. Intimal streak
B. Intimal tear
C. Medial degeneration
D. Medial inflammation
E. Vasa vasorum obliteration

Submit

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A. Intimal streak (2%)
B. Intimal tear (7%)
C. Medial degeneration (6%)
D. Medial inflammation (10%)
E. Vasa vasorum obliteration (72%)

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This patient's murmur is characteristic of **aortic regurgitation**, which, in the presence of mediastinal widening, suggests an **aortic aneurysm** that has dilated the aortic annulus. The positive serology for **syphilis** (positive fluorescent treponemal antibody absorption [FTA-ABS] test) suggests a "luetic" aneurysm, consistent with tertiary syphilis.

Tertiary syphilis begins with **vasa vasorum endarteritis** and obliteration, resulting in inflammation, ischemia, and weakening of the adventitia. Aneurysmal dilation of the thoracic aorta results and can extend to involve the aortic valve ring. Syphilitic aneurysms are uncommon in the United States.

(Choice A) Intimal streaks are the earliest lesions of atherosclerosis. Severe, complicated intimal atheromas can destroy and weaken the underlying media, resulting in aortic aneurysms. However, the most common site of these lesions is in the abdominal aorta (below the origin of the renal arteries). Although atherosclerosis can promote aneurysm formation in the thoracic aorta, the positive FTA-ABS test makes atherosclerosis less likely to be the cause of this patient's symptoms.

(Choices B and C) Intimal tear and medial degeneration (elastic tissue fragmentation and separation of the elastic and fibromuscular components of the tunica media by small, cleft-like spaces) are common histopathologic abnormalities seen with aortic dissections (severe chest pain radiating to the back), not

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makes atherosclerosis less likely to be the cause of this patient's symptoms.

(Choices B and C) Intimal tear and medial degeneration (elastic tissue fragmentation and separation of the elastic and fibromuscular components of the tunica media by small, cleft-like spaces) are common histopathologic abnormalities seen with aortic dissections (severe chest pain radiating to the back), not aortic aneurysms.

(Choice D) Large vessel arteritides with medial inflammation (eg, Takayasu, giant cell arteritis) might rarely promote an aortic aneurysm; however, they are not associated with a positive serology for syphilis.

Educational objective:
Tertiary syphilis can result in thoracic aortic aneurysm. If the aneurysm compresses adjacent structures and dilates the aortic valve ring, a murmur and mediastinal widening might be present. The pathogenesis begins with vasa vasorum endarteritis and obliteration, resulting in inflammation, ischemia, and weakening of the aortic adventitia. Fluorescent treponemal antibody absorption testing is specific for syphilis.

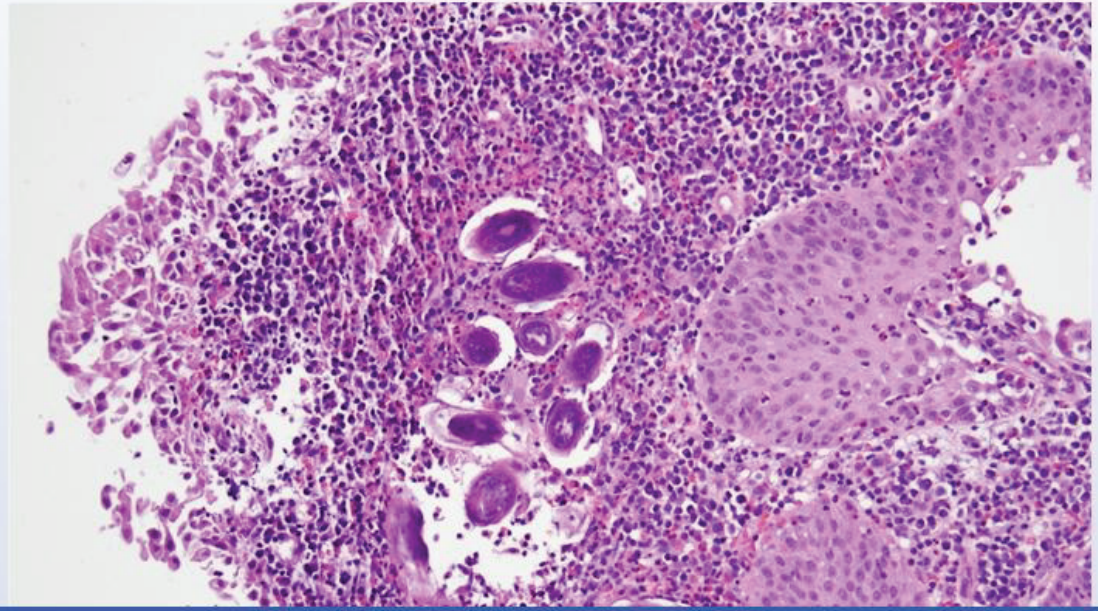
Pathology	Infectious Diseases	Syphilis
Subject	System	Topic

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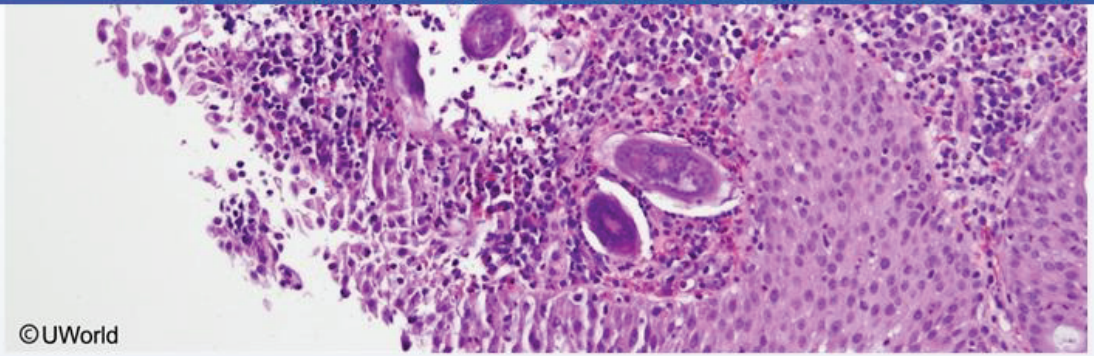
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A 54-year-old Sudanese immigrant is evaluated for several months of intermittent dysuria and gross hematuria. The patient notes that he passes blood at the end of urination but has no associated pain. Cystoscopy reveals erythematous areas in the bladder mucosa. Multiple biopsies are taken from the affected sites; histopathological findings are shown in the image below.



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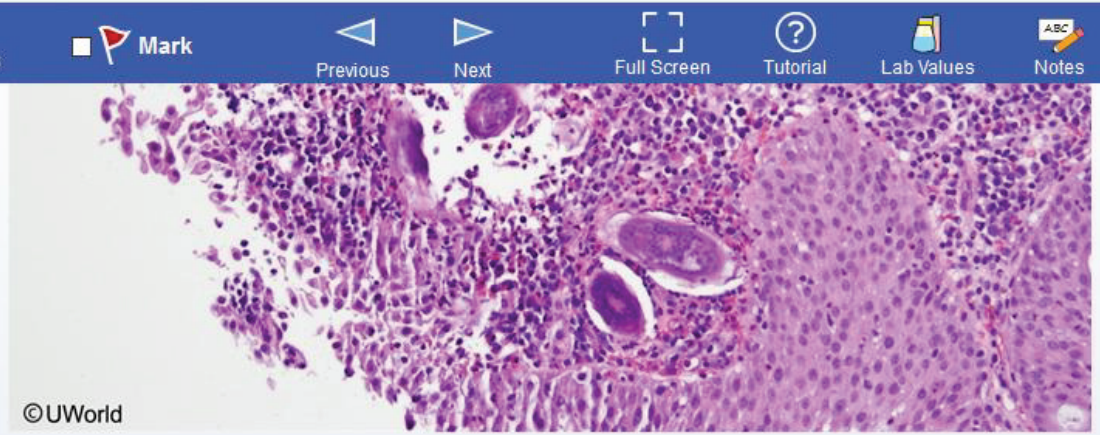
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Which of the following most likely predisposed this patient to his current condition?

A. Chronic urinary tract obstruction
B. Contaminated water exposure
C. Cytotoxic immunosuppressant use
D. Extensive cigarette smoking
E. Urea-splitting bacterial infection

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Which of the following most likely predisposed this patient to his current condition?

A. Chronic urinary tract obstruction (3%)

✓ B. Contaminated water exposure (77%)

C. Cytotoxic immunosuppressant use (2%)

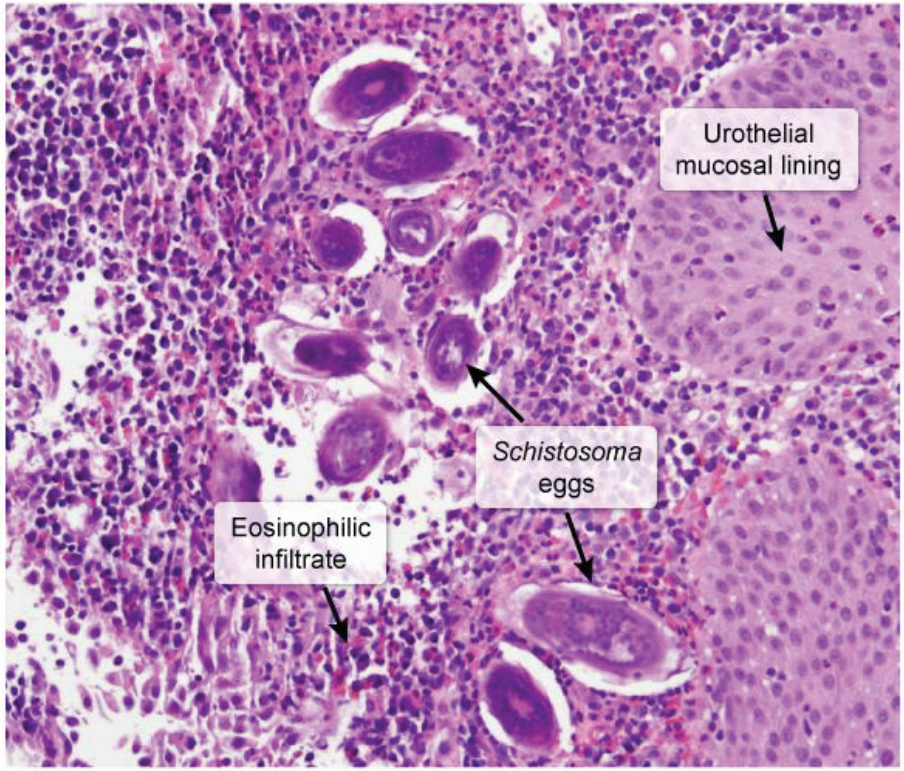
D. Extensive cigarette smoking (14%)

E. Urea-splitting bacterial infection (3%)

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Urinary schistosomiasis



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Schistosomiasis is a parasitic blood fluke infection endemic to rural areas of sub-Saharan Africa, Asia, and South America. Transmission occurs when humans **bathe in freshwater** ponds, lakes, or rivers contaminated with cercariae from **infected snails**. Cercariae penetrate the dermis and travel to the liver, where they evolve into adult worms and subsequently migrate into the venules in the walls of the intestines, colon, or bladder.

Because adult schistosomes absorb host proteins and display host antigens on their surface, they are relatively protected from immune recognition and generally do not cause symptoms. However, adult worms shed **eggs** into the circulation that travel through host tissues and induce **eosinophilic granulomatous inflammation** and fibrosis (as seen in the image above). This can lead to indolent symptoms in the liver, spleen, bowel wall, and genitourinary system. One characteristic manifestation of genitourinary schistosomiasis is the development of hematuria at the end of voiding **("terminal hematuria")** due to bladder wall inflammation and ulcers; urinary calcifications, obstruction, and bladder cancer may eventually develop.

(Choice A) Benign prostatic hyperplasia can cause chronic urinary tract obstruction. Patients usually have difficulty voiding urine (eg, slow stream, hesitancy), frequency, urgency, and/or nocturia.

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(Choice A) Benign prostatic hyperplasia can cause chronic urinary tract obstruction. Patients usually have difficulty voiding urine (eg, slow stream, hesitancy), frequency, urgency, and/or nocturia.

(Choice C) Cyclophosphamide is a common cause of hemorrhagic cystitis in patients undergoing chemotherapy for cancer or chronic rheumatologic conditions. Cystoscopy may show bladder irritation, but eggs would not be seen on biopsy.

(Choice D) Cigarette smoking is a major risk factor for the development of bladder cancer (usually transitional cell carcinoma), which classically presents with painless hematuria. However, cystoscopy generally shows a mass, and biopsy would reveal malignant cells, not eggs.

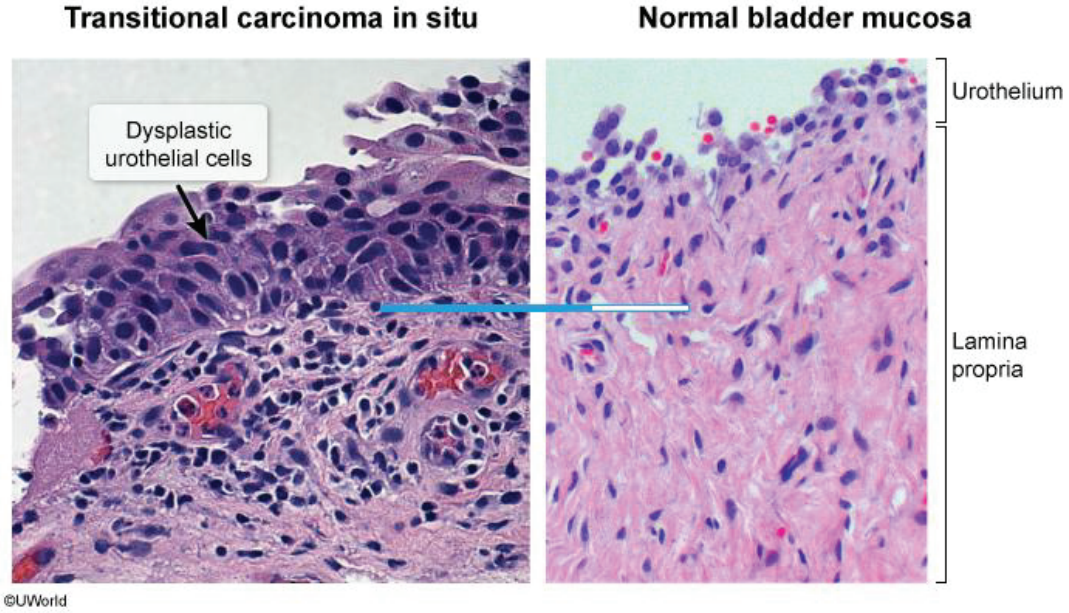
(Choice E) Genitourinary infections with bacteria that split urea such as *Proteus mirabilis* are frequently associated with the formation of urinary stones. Nephrolithiasis can cause hematuria but is usually very painful.

Educational objective:
Schistosomiasis is a parasitic blood fluke infection that is associated with bathing in freshwater contaminated with cercariae from infected snails. Patients often are asymptomatic for months or years but may eventually develop eosinophilic granulomatous inflammation in the liver, spleen, gastrointestinal tract, or genitourinary system. One common manifestation of genitourinary schistosomiasis is painless terminal

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or genitourinary system. One common manifestation of genitourinary schistosomiasis is painless terminal

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chemotherapy for cancer or chronic rheumatologic conditions. Cystoscopy may show bladder irritation, but eggs would not be seen on biopsy.

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(Choice E) Genitourinary infections with bacteria that split urea such as *Proteus mirabilis* are frequently associated with the formation of urinary stones. Nephrolithiasis can cause hematuria but is usually very painful.

Educational objective:

Schistosomiasis is a parasitic blood fluke infection that is associated with bathing in freshwater contaminated with cercariae from infected snails. Patients often are asymptomatic for months or years but may eventually develop eosinophilic granulomatous inflammation in the liver, spleen, gastrointestinal tract, or genitourinary system. One common manifestation of genitourinary schistosomiasis is painless terminal hematuria; eggs can often be identified in the urine or on biopsy.

Pathology	Infectious Diseases	Schistosomiasis
Subject	System	Topic

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A 26-year-old man develops dysuria and purulent urethral discharge following unprotected sex with a new partner. Nucleic acid amplification testing is positive for *Neisseria gonorrhoeae* infection. The patient develops antibody against the bacterial pili that enhance attachment to host cells. His symptoms resolve with adequate treatment. His partner does not receive treatment. Several weeks later, the patient develops *N gonorrhoeae* reinfection after repeat exposure to the same partner. Which of the following is the most likely reason for the lack of long-lasting immunity against the bacteria despite antibody formation in this patient?

A. Antigenic mimicry
B. Antigenic variation
C. Conjugative plasmid
D. Low molecular weight antigen
E. Non-protein antigen

Submit

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A 26-year-old man develops dysuria and purulent urethral discharge following unprotected sex with a new partner. Nucleic acid amplification testing is positive for *Neisseria gonorrhoeae* infection. The patient develops antibody against the bacterial pili that enhance attachment to host cells. His symptoms resolve with adequate treatment. His partner does not receive treatment. Several weeks later, the patient develops *N gonorrhoeae* reinfection after repeat exposure to the same partner. Which of the following is the most likely reason for the lack of long-lasting immunity against the bacteria despite antibody formation in this patient?

A. Antigenic mimicry (1%)
B. Antigenic variation (87%)
C. ~~Conjugative plasmid~~ (4%)
D. ~~Low molecular weight antigen~~ (0%)
E. ~~Non-protein antigen~~ (4%)

87%
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Many strains of *Neisseria gonorrhoeae* have pili, hair-like protein polymers projecting from the bacterial surface that are involved in organism attachment to mucosal surfaces. When the host produces antibodies against gonococcal pili, mucosal adherence is inhibited. At a given time, only 1 pilus gene is functional, so only 1 pilus type is expressed. However, the structural genes for pilus proteins undergo **antigenic variation** at a high frequency; they undergo **recombination** with each other to produce new antigenic types of pili. The number of possible antigenic pilus types is theoretically quite large. This diversity is a reason that vaccine development against *N gonorrhoeae* pili has been challenging.

(Choice A) Antigenic mimicry is the sharing of antigenic sequences between the microorganism and the host cell, facilitating immune evasion. The gonococcal lipooligosaccharide is similar in structure to human cell membrane glycosphingolipids. However, this is not related to antibody formation against the pilus. Antigenic mimicry can lead to autoimmune disease if the host mounts an immune response against the infectious epitope and that epitope has sufficient sequence homology with a host antigen.

(Choice C) Plasmid conjugation plays an important role in gonococcal antibiotic resistance.

(Choice D) Pilin proteins do not represent a low molecular weight structure that would be poorly immunogenic.

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Antigenic mimicry can lead to autoimmune disease if the host mounts an immune response against the infectious epitope and that epitope has sufficient sequence homology with a host antigen.

(Choice C) Plasmid conjugation plays an important role in gonococcal antibiotic resistance.

(Choice D) Pilin proteins do not represent a low molecular weight structure that would be poorly immunogenic.

(Choice E) Gonococcal pili are protein polymers. In addition, vaccines have been developed against non-protein structures (eg, meningococcal vaccine, pneumococcal vaccine).

Educational objective:

Gonococci use their pili to mediate adherence to the mucosal epithelium. Through antigenic variation, each gonococcus can modify the pilus protein expressed, thereby avoiding host defenses (to some degree) and making vaccination directed against the pilus protein difficult.

Microbiology	Infectious Diseases	Gonococcal infection
Subject	System	Topic

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Studies conducted following an influenza epidemic that affected the inhabitants of several countries determine that the cause is an antigenically novel virus strain carrying the animal-strain hemagglutinin and neuraminidase surface molecules. Further analysis reveals that reassortment of the genetic materials occurred during coinfection with human influenza virus and swine influenza virus, leading to the development of some progeny that contain genetic materials from both viruses. Which of the following viruses can undergo a similar process?

A. Hepatitis C virus
B. Human papillomavirus
C. Measles virus
D. Poliovirus
E. Rotavirus

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Studies conducted following an influenza epidemic that affected the inhabitants of several countries determine that the cause is an antigenically novel virus strain carrying the animal-strain hemagglutinin and neuraminidase surface molecules. Further analysis reveals that reassortment of the genetic materials occurred during coinfection with human influenza virus and swine influenza virus, leading to the development of some progeny that contain genetic materials from both viruses. Which of the following viruses can undergo a similar process?

A. Hepatitis C virus (19%)
B. Human papillomavirus (9%)
C. Measles virus (10%)
D. Poliovirus (5%)
✓ E. Rotavirus (55%)

Correct

55%
Answered correctly

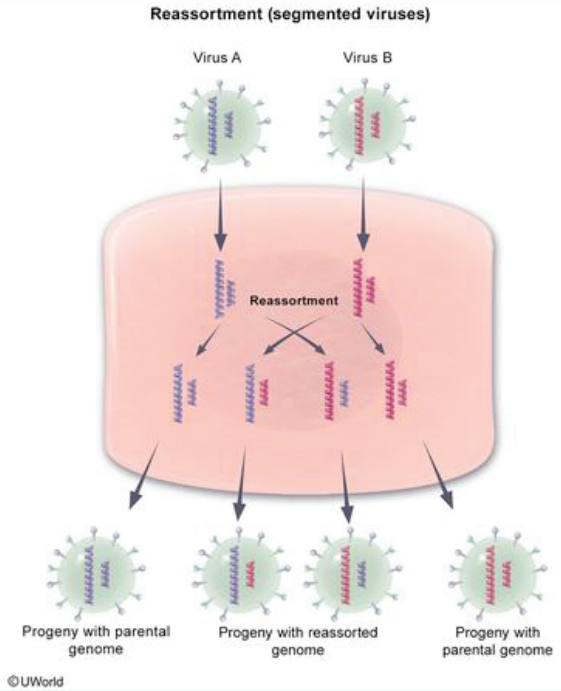
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Genetic shift in the influenza A virus involves **reassortment** of genomic segments of the **human** strain with genomic segments of the **animal** strain, typically when both strains coinfect birds (avian) or pigs (swine). The resulting new strain can cause a new influenza epidemic or pandemic if it has dramatically altered viral surface glycoproteins (eg, hemagglutinin).

The key structural feature that enables influenza viruses to undergo such relatively rapid genetic shifts through reassortment is the **segmented** nature of their genomes. Members of another virus family with a segmented genome could also undergo such reassortment - as opposed to the less radical, slower genetic drift that occurs via point mutations in all viral families. Among the viruses listed, only **rotavirus** has a segmented genome. Segmented viruses include orthomyxoviruses, reoviruses, bunyaviruses, and arenaviruses.

(Choices A, B, C, and D) Hepatitis C virus, human papillomavirus, measles virus, and poliovirus all lack the segmented genome necessary to undergo reassortment.

Educational objective:
Viruses with segmented genomes (eg, orthomyxoviruses, rotaviruses) are capable of genetic shifts through reassortment. Reassortment (genetic shift) involves exchange of entire genomic segments, a far more dramatic process than the point mutations responsible for genetic drift.

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A 23-year-old man is hospitalized for fever, headache, and confusion. He does not use tobacco or illicit drugs and is monogamous with his wife. The patient's cerebrospinal fluid analysis reveals lymphocytic pleocytosis, and a PCR is positive for herpesvirus. The patient is treated with intravenous high-dose acyclovir. Fever and mental status gradually improve, but on the third day of hospitalization the patient's serum creatinine level increases to 3.4 mg/dL from a baseline of 0.9 mg/dL at admission. The observed finding could have been prevented by which of the following?

A. Aggressive intravenous hydration
B. Careful taking of allergy history
C. Monitoring of blood drug levels
D. Pretreatment with allopurinol
E. Pretreatment with prednisone

Submit

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A 23-year-old man is hospitalized for fever, headache, and confusion. He does not use tobacco or illicit drugs and is monogamous with his wife. The patient's cerebrospinal fluid analysis reveals lymphocytic pleocytosis, and a PCR is positive for herpesvirus. The patient is treated with intravenous high-dose acyclovir. Fever and mental status gradually improve, but on the third day of hospitalization the patient's serum creatinine level increases to 3.4 mg/dL from a baseline of 0.9 mg/dL at admission. The observed finding could have been prevented by which of the following?

- ✓ A. Aggressive intravenous hydration (67%)
- B. Careful taking of allergy history (3%)
- C. Monitoring of blood drug levels (16%)
- D. Pretreatment with allopurinol (7%)
- E. Pretreatment with prednisone (5%)

Correct

67% Answered correctly

37 secs Time Spent

02/10/2021 Last Updated

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The acute elevation of this patient's serum creatinine on the third day of hospitalization is likely due to **acyclovir nephrotoxicity**, which occurs in 5%-10% of patients who receive the drug intravenously. Acyclovir is excreted principally in the urine via glomerular filtration and tubular secretion. When the acyclovir concentration in the collecting duct exceeds its solubility, crystallization, crystalluria, and renal tubular damage can occur. In most cases, this toxic complication is transient and can be prevented (as well as treated) with **adequate hydration** and a reduction in the rate of drug infusion.

(Choice B) Acute interstitial nephritis (AIN) is an allergic inflammation of the kidney that is most commonly triggered by medications and is often associated with fever, rash, and eosinophilia. However, acyclovir is not a common cause of AIN; common causes include nonsteroidal anti-inflammatory drugs, penicillins, cephalosporins, diuretics, and allopurinol.

(Choice C) Monitoring of acyclovir blood levels is not always effective in preventing nephrotoxicity. During states of low intravascular volume (eg, dehydration), nephrotoxicity can develop secondary to increased urinary concentration even when acyclovir blood levels are not within the established toxic range.

(Choice D) Allopurinol blocks xanthine oxidase, which reduces the formation of uric acid. Pretreatment with allopurinol is often used in patients with lymphoma and leukemia to prevent urate crystal nephropathy due to tumor lysis syndrome. Acyclovir nephrotoxicity is mediated by the formation of acyclovir crystals,

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(Choice E) Pretreatment with prednisone can help prevent radiocontrast-induced allergic reactions. Prednisone does not prevent the formation of acyclovir crystals.

Educational objective:
Intravenous acyclovir can cause crystalline nephropathy if adequate hydration is not also provided.

Pharmacology	Infectious Diseases	Acyclovir
Subject	System	Topic

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A 65-year-old man comes to the emergency department due to fevers, chills, and confusion. He has a history of poorly controlled diabetes mellitus with a nonhealing ulcer of the left foot. His temperature is 38.3 C (101 F), blood pressure is 90/60 mm Hg, pulse is 112/min, and respirations are 22/min. On examination, there is slight erythema surrounding his left foot ulcer with foul-smelling discharge. No heart murmur is auscultated, the lungs are clear, and the abdomen is soft and nontender. Blood cultures are obtained, and he is started on broad-spectrum antibiotics. Twenty-four hours later, blood cultures grow β-lactamase-producing *Bacteroides* species. Which of the following is most likely to provide appropriate antimicrobial coverage for this patient?

A. Azithromycin
B. Ceftriaxone
C. Ciprofloxacin
D. Piperacillin-tazobactam
E. Vancomycin

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history of poorly controlled diabetes mellitus with a nonhealing ulcer of the left foot. His temperature is 38.3 C (101 F), blood pressure is 90/60 mm Hg, pulse is 112/min, and respirations are 22/min. On examination, there is slight erythema surrounding his left foot ulcer with foul-smelling discharge. No heart murmur is auscultated, the lungs are clear, and the abdomen is soft and nontender. Blood cultures are obtained, and he is started on broad-spectrum antibiotics. Twenty-four hours later, blood cultures grow β-lactamase-producing *Bacteroides* species. Which of the following is most likely to provide appropriate antimicrobial coverage for this patient?

A. Azithromycin (9%)
B. Ceftriaxone (10%)
C. Ciprofloxacin (14%)
D. Piperacillin-tazobactam (51%)
E. Vancomycin (14%)

Correct
51%
01 min, 03 secs
11/07/2020

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Areas of necrosis and diminished blood supply (such as chronic, nonhealing ulcers) facilitate the growth of anaerobes. ***Bacteroides*** are gram-negative **anaerobic** rods that can produce β-lactamase, an enzyme that breaks down penicillins. **β-lactamase inhibitors** such as tazobactam, clavulanic acid, and sulbactam prevent these enzymes from functioning. The **combination** of piperacillin (extended-spectrum penicillin) and tazobactam is effective against a large number of gram-positive, gram-negative, and anaerobic bacteria and would be the most appropriate option among the medications listed. Other antimicrobials with anaerobic activity include metronidazole, carbapenems, and clindamycin (in most cases). In patients with diabetes who have a necrotic (foul-smelling) infected ulcer, broad-spectrum antimicrobial coverage should be used as polymicrobial infection with organisms other than *Bacteroides* may be present.

(Choice A) Azithromycin is a macrolide antibiotic that binds to the 50S subunit of bacteria ribosomes, thereby inhibiting protein synthesis. It is used for infections with *Chlamydia, Mycoplasma, Haemophilus influenzae,* and *Moraxella catarrhalis*. Anaerobic activity against many *Fusobacterium* and some *Bacteroides* species may be limited.

(Choice B) Ceftriaxone is a third-generation parenteral cephalosporin with poor anaerobic activity. It is active against *H influenzae, Klebsiella pneumoniae*, and *Neisseria* and *Serratia* species.

(Choice C) Ciprofloxacin is a second-generation quinolone that acts by interfering with bacterial DNA

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(Choice C) Ciprofloxacin is a second-generation quinolone that acts by interfering with bacterial DNA gyrase (topoisomerase II). Ciprofloxacin is active against most gram-negative rods and bacilli, including *Legionella* and *Pseudomonas aeruginosa*. It is not effective against anaerobic infections.

(Choice E) Vancomycin is a tricyclic glycopeptide that inhibits the synthesis of peptidoglycan, a main component of the cell wall of gram-positive bacteria. It is used against methicillin-resistant *Staphylococcus aureus* as well as *Clostridium difficile*.

Educational objective:
Piperacillin-tazobactam is a combination of extended-spectrum penicillin with β-lactamase inhibitor. It is effective against most gram-negative enteric rods (including *Pseudomonas aeruginosa*) and against *Bacteroides fragilis*.

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A 78-year-old woman comes to the office due to fever, headache, sore throat, cough, and severe myalgias for 24 hours. Her medical problems include hypertension and Alzheimer dementia. Her family came to visit over the weekend, and her grandson had symptoms of a cold. The patient's temperature is 38.9 C (102 F). Lung examination is unremarkable. A nasal specimen swab is positive for influenza. The patient is started on oseltamivir. Which of the following is most likely impaired in the patient's infected cells as a result of the treatment?

A. Foreign protein splitting
B. Foreign protein synthesis
C. Viral RNA replication
D. Viral uncoating
E. Virion particle release

Submit

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A 78-year-old woman comes to the office due to fever, headache, sore throat, cough, and severe myalgias for 24 hours. Her medical problems include hypertension and Alzheimer dementia. Her family came to visit over the weekend, and her grandson had symptoms of a cold. The patient's temperature is 38.9 C (102 F). Lung examination is unremarkable. A nasal specimen swab is positive for influenza. The patient is started on oseltamivir. Which of the following is most likely impaired in the patient's infected cells as a result of the treatment?

A. Foreign protein splitting (2%)
B. Foreign protein synthesis (3%)
C. Viral RNA replication (12%)
D. Viral uncoating (13%)
✓ E. Virion particle release (67%)

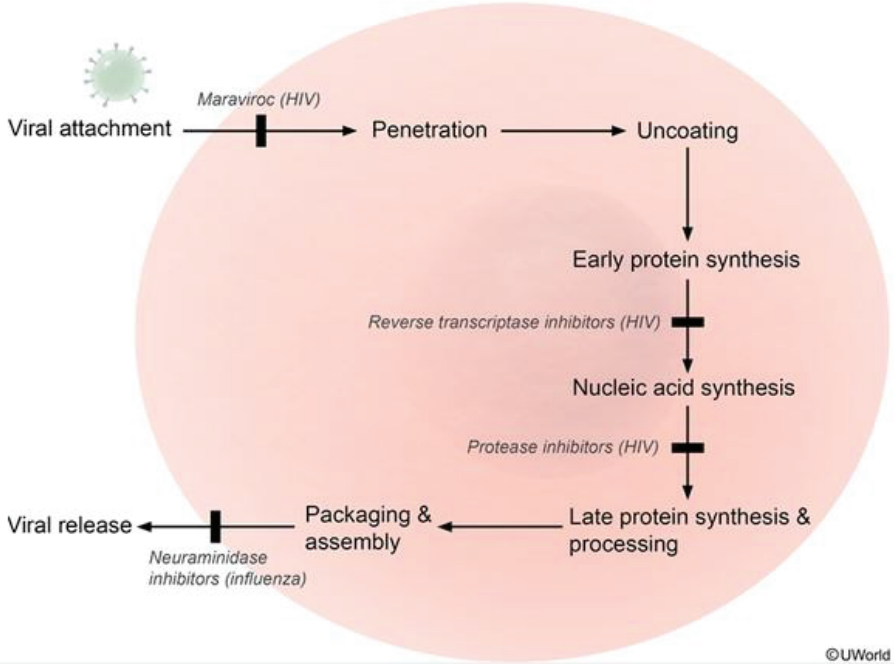
Correct
67% Answered correctly
26 secs Time Spent
10/10/2020 Last Updated

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Exhibit Display

Viral replication cycle & antiviral therapy



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Neuraminidase

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Oseltamivir is a **neuraminidase inhibitor** useful in the treatment of both influenza A and B virus infections. Neuraminidase is required for the **release** of virus from infected cells and for the spread of virus within the respiratory tract. Neuraminidase inhibitors cause the newly synthesized virions to adhere to the host cell surface and form viral aggregates, thereby reducing the spread of virus to other host cells. Oseltamivir (Tamiflu) can shorten the course and complications of influenza A and B infections if taken within 48 hours of the onset of symptoms. In addition, oseltamivir works to slow viral penetration of the mucous secretions that protect the respiratory epithelium. Oseltamivir can therefore be used to treat or prevent influenza.

(Choice A) The influenza viral genome consists of segmented RNA, which is translated predominantly into individual proteins rather than a large polyprotein product. HIV protease inhibitors (eg, darunavir) are used to counteract HIV polyprotein cleavage mediated by viral protease.

(Choice B) Foreign (viral) protein synthesis can be inhibited by α- and β-interferons, which induce the synthesis of proteins that have an antiviral effect. These antiviral proteins promote the degradation of RNA and halt protein translation in virally infected cells only.

(Choice C) Impairment of viral RNA replication is accomplished by the reverse transcriptase inhibitors

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synthesis of proteins that have an antiviral effect. These antiviral proteins promote the degradation of RNA and halt protein translation in virally infected cells only.

(Choice C) Impairment of viral RNA replication is accomplished by the reverse transcriptase inhibitors used to combat HIV (eg, abacavir, tenofovir, zidovudine).

(Choice D) Amantadine (limited use in influenza management due to viral resistance) impairs uncoating or disassembly of the influenza A virion after host cell endocytosis. Oseltamivir does not operate via the same mechanism of action. Currently, amantadine is mainly used in Parkinson disease as it increases dopamine release (unclear mechanism).

Educational objective:
Oseltamivir is a neuraminidase inhibitor useful in the treatment and prevention of both influenza A and B virus infections. This medication impairs the release of newly formed virions from infected host cells and impairs viral penetration of mucous secretions that overlie the respiratory epithelium.

Pharmacology	Infectious Diseases	Influenza
Subject	System	Topic

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A 32-year-old man comes to the office due to an acute febrile illness that developed after a deer-hunting trip in Arkansas. The patient recalls getting tick bites in the woods but initially had no symptoms. He began experiencing fever, chills, malaise, headache, and myalgia a week after his return. Physical examination shows a diffuse, maculopapular rash; clear oropharynx; normal lung and heart sounds; and mild, diffuse abdominal tenderness. Laboratory testing reveals leukopenia, thrombocytopenia, and elevated aminotransferase levels. Microscopic evaluation of the blood demonstrates mulberry-shaped, intracytoplasmic inclusions in monocytes. Which of the following is the most likely pathogen responsible for this patient's condition?

A. *Babesia microti*
B. *Borrelia burgdorferi*
C. *Ehrlichia chaffeensis*
D. *Francisella tularensis*
E. *Rickettsia rickettsii*

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trip in Arkansas. The patient recalls getting tick bites in the woods but initially had no symptoms. He began experiencing fever, chills, malaise, headache, and myalgia a week after his return. Physical examination shows a diffuse, maculopapular rash; clear oropharynx; normal lung and heart sounds; and mild, diffuse abdominal tenderness. Laboratory testing reveals leukopenia, thrombocytopenia, and elevated aminotransferase levels. Microscopic evaluation of the blood demonstrates mulberry-shaped, intracytoplasmic inclusions in monocytes. Which of the following is the most likely pathogen responsible for this patient's condition?

A. *Babesia microti* (16%)

B. ~~*Borrelia burgdorferi*~~ (8%)

C. *Ehrlichia chaffeensis* (44%)

D. ~~*Francisella tularensis*~~ (8%)

E. ~~*Rickettsia rickettsii*~~ (22%)

Correct

44%

02 mins, 58 secs

03/05/2021

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Ehrlichia chaffeensis is harbored by **white-tailed deer** in the southwestern, southeastern, and mid-Atlantic United States. It is transmitted to humans by **tick bite** (eg, lone star tick) and subsequently spreads to tissue rich in **mononuclear cells** (eg, bone marrow, lymph nodes, liver, spleen), leading to nonspecific symptoms (eg, fever, chills, myalgia, headache), maculopapular rash, and significant laboratory abnormalities (eg, **lymphopenia**, thrombocytopenia, elevated aminotransferases).

E chaffeensis replicates in membrane-bound vacuoles within the cytoplasm of monocytes and can be visualized on peripheral blood or buffy coat examination as **mulberry-shaped, intraleukocytic inclusions** (morulae). Treatment with antibiotics (eg, doxycycline) is usually curative.

(Choice A) *Babesia* is a protozoa transmitted by ticks in the northeastern and midwestern United States. It appears as a ring-shaped, intraerythrocytic parasite (similar to *Plasmodium*).

(Choice B) *Borrelia burgdorferi* causes Lyme disease and is transmitted by ticks (eg, *Ixodes scapularis*). Initial infection usually causes nonspecific symptoms (eg, fatigue, headache, myalgia) and a spreading, annular rash called erythema migrans. However, *B burgdorferi* is not typically visualized on microscopy and does not replicate in membrane-bound inclusions.

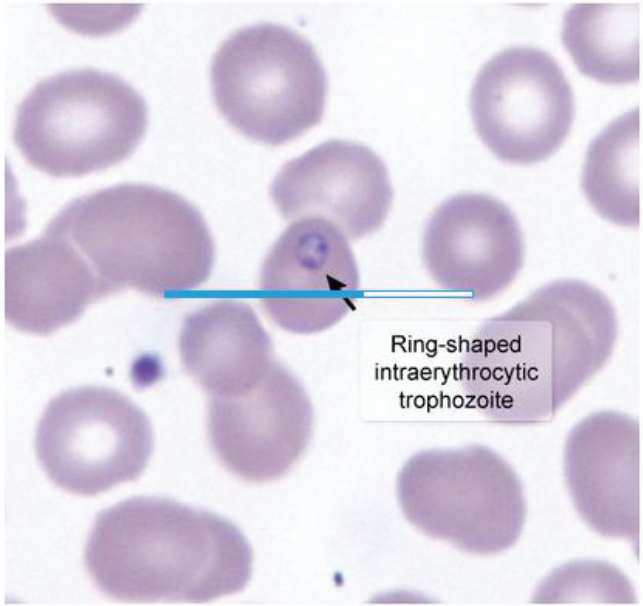
(Choice D) *Francisella tularensis* is an aerobic, gram-negative bacterium that is transmitted when humans come into contact with infected animals (eg, rabbits). It causes tularemia, which is typically characterized

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Babesia



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come into contact with infected animals (eg, rabbits). It causes tularemia, which is typically characterized

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and does not replicate in membrane-bound inclusions.

(Choice D) *Francisella tularensis* is an aerobic, gram-negative bacterium that is transmitted when humans come into contact with infected animals (eg, rabbits). It causes tularemia, which is typically characterized by tender, regional lymphadenopathy and a single, papulo-ulcerative lesion with eschar. This pathogen does not grow within membrane-bound vacuoles within leukocytes.

(Choice E) *Rickettsia rickettsii* is a tick-borne, gram-negative, obligate, intracellular bacterium that attacks vascular endothelial cells and causes Rocky Mountain spotted fever. Patients typically develop nonspecific symptoms (eg, fever, headache, myalgia) followed by a blanching, erythematous, centripetal rash that begins on the ankles and wrists.

Educational objective:
Ehrlichia chaffeensis is harbored in white-tailed deer and transmitted to humans by tick bite. It replicates in vacuoles within monocytes and forms mulberry-shaped, intraleukocytic inclusions (morulae). Manifestations usually include nonspecific symptoms (eg, fever, chills, myalgia), maculopapular rash, and significant laboratory abnormalities, particularly lymphopenia.

Microbiology	Infectious Diseases	Ehrlichiosis & anaplasmosis
Subject	System	Topic

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Researchers analyze the HIV viral structure and replication cycle for new drug targets. They find the virus encodes a large glycoprotein, which gets cleaved into 2 subunits, the surface and transmembrane subunits. These subunits remain noncovalently bound to each other in the virion. Upon activation of the surface protein, conformational changes occur in the transmembrane subunit exposing the functional inner core. A novel drug is developed that selectively binds and prevents normal functioning of the transmembrane subunit, interfering with the normal viral replication cycle. This agent most likely directly inhibits which of the following viral processes?

A. Attachment of the virus to target cell surface
B. Budding and release of a new virus particle
C. Cleavage of polyproteins by viral encoded enzyme
D. Entry of the viral core into host cytoplasm
E. Integration of the viral DNA into host genome
F. Synthesis of DNA from viral RNA template
G. Transcription of mRNA from proviral DNA

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encodes a large glycoprotein, which gets cleaved into 2 subunits, the surface and transmembrane subunits. These subunits remain noncovalently bound to each other in the virion. Upon activation of the surface protein, conformational changes occur in the transmembrane subunit exposing the functional inner core. A novel drug is developed that selectively binds and prevents normal functioning of the transmembrane subunit, interfering with the normal viral replication cycle. This agent most likely directly inhibits which of the following viral processes?

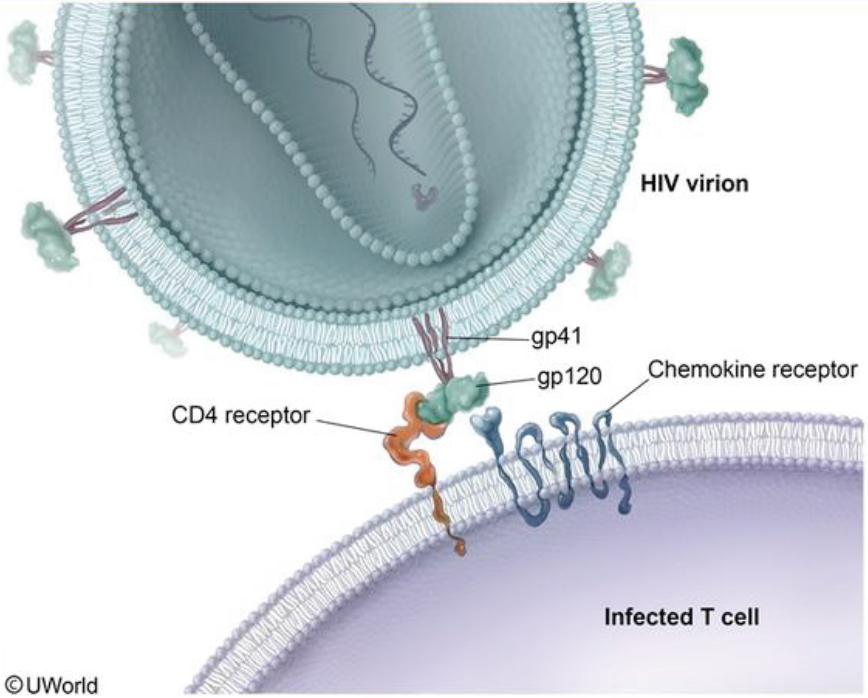
A. ~~Attachment of the virus to target cell surface~~ (20%)
B. ~~Budding and release of a new virus particle~~ (4%)
C. ~~Cleavage of polyproteins by viral encoded enzyme~~ (4%)
✓ D. Entry of the viral core into host cytoplasm (57%)
E. ~~Integration of the viral DNA into host genome~~ (7%)
F. ~~Synthesis of DNA from viral RNA template~~ (3%)
G. ~~Transcription of mRNA from proviral DNA~~ (1%)

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Explanation

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The HIV genome encodes several enzymes and structural proteins in polycistronic mRNAs that are then translated into polyproteins and cleaved by proteases into the individual proteins that compose the virus. The *env* gene encodes the **polyprotein gp160**, which is extensively **glycosylated** in the endoplasmic reticulum and Golgi body and subsequently cleaved into the mature envelope proteins gp120 and gp41. These envelope proteins remain associated by noncovalent attachments and form the **glycoprotein spikes** that pepper the surface of the HIV virus.

gp120 forms the outside surface of the glycoprotein spike and **mediates viral attachment** to the host cell by binding with the CD4 receptor and a chemokine coreceptor (CXCR4, CCR5) **(Choice A)**. Binding of gp120 to these host receptors induces a conformational change in the structure of the glycoprotein spike that exposes the underlying transmembrane glycoprotein gp41. **gp41 mediates fusion** of the viral cell membrane with the host cell membrane, thereby allowing the **viral core to enter the cell**.

Drugs that selectively bind gp41 (eg, enfuvirtide) are known as **fusion inhibitors** because they prevent gp41 from undergoing the conformational changes necessary for viral fusion, which prevents the HIV genome from entering uninfected cells.

(Choice B) Viral assembly and budding occur at the cell surface. The envelope proteins (gp120, gp41)

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genome from entering uninfected cells.

(Choice B) Viral assembly and budding occur at the cell surface. The envelope proteins (gp120, gp41) are expressed on the cell surface and then a complex of the nucleocapsid, viral RNA, and viral proteins (gag and pol polyproteins) bud from the surface. Further assembly then occurs when the virus is free from the host cell. The transmembrane gp41 does not catalyze the budding or assembly process.

(Choice C) Protease is an HIV enzyme that mediates the cleavage of HIV polyproteins into the individual proteins that compose the HIV virus. Protease inhibitors (eg, atazanavir, darunavir) block the action of this enzyme.

(Choice E) Integrase inserts the viral double-stranded DNA into the host genome. Inte*gra*se inhibitors (eg, ralte*gra*vir, dolute*gra*vir) are often part of first-line therapy for HIV.

(Choice F) Reverse transcriptase converts viral single-stranded RNA into complementary double-stranded DNA. Reverse transcriptase inhibitors terminate viral DNA elongation by competitive or allosteric inhibition.

(Choice G) Host RNA polymerase II transcribes proviral DNA into mRNA, which is then translated in the rough endoplasmic reticulum.

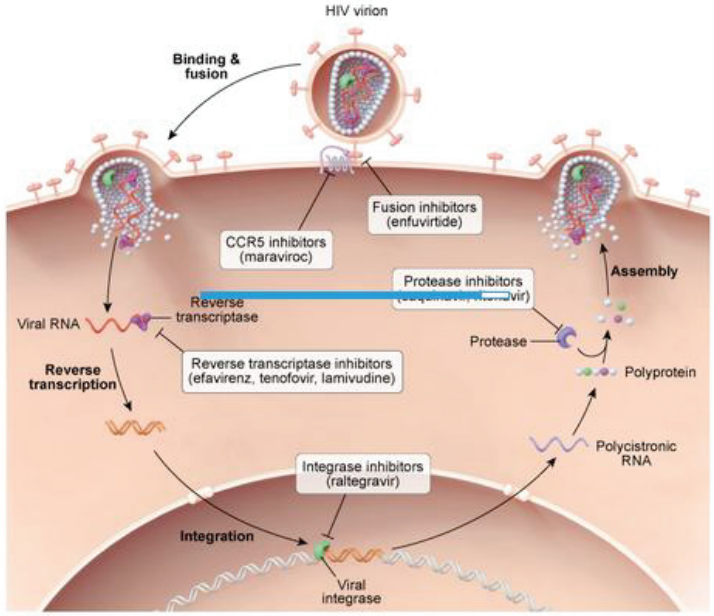
Educational objective:

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HIV antiviral drugs



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(Choice C) Protease is an HIV enzyme that mediates the cleavage of HIV polyproteins into the individual proteins that compose the HIV virus. Protease inhibitors (eg, atazanavir, darunavir) block the action of this enzyme.

(Choice E) Integrase inserts the viral double-stranded DNA into the host genome. Inte*gra*se inhibitors (eg, ralte*gra*vir, dolute*gra*vir) are often part of first-line therapy for HIV.

(Choice F) Reverse transcriptase converts viral single-stranded RNA into complementary double-stranded DNA. Reverse transcriptase inhibitors terminate viral DNA elongation by competitive or allosteric inhibition.

(Choice G) Host RNA polymerase II transcribes proviral DNA into mRNA, which is then translated in the rough endoplasmic reticulum.

Educational objective:
Fusion inhibitors (eg, enfuvirtide) bind the HIV transmembrane glycoprotein gp41 and prevent it from approximating the viral and host cellular membranes, which prevents HIV penetration into new host cells.

References

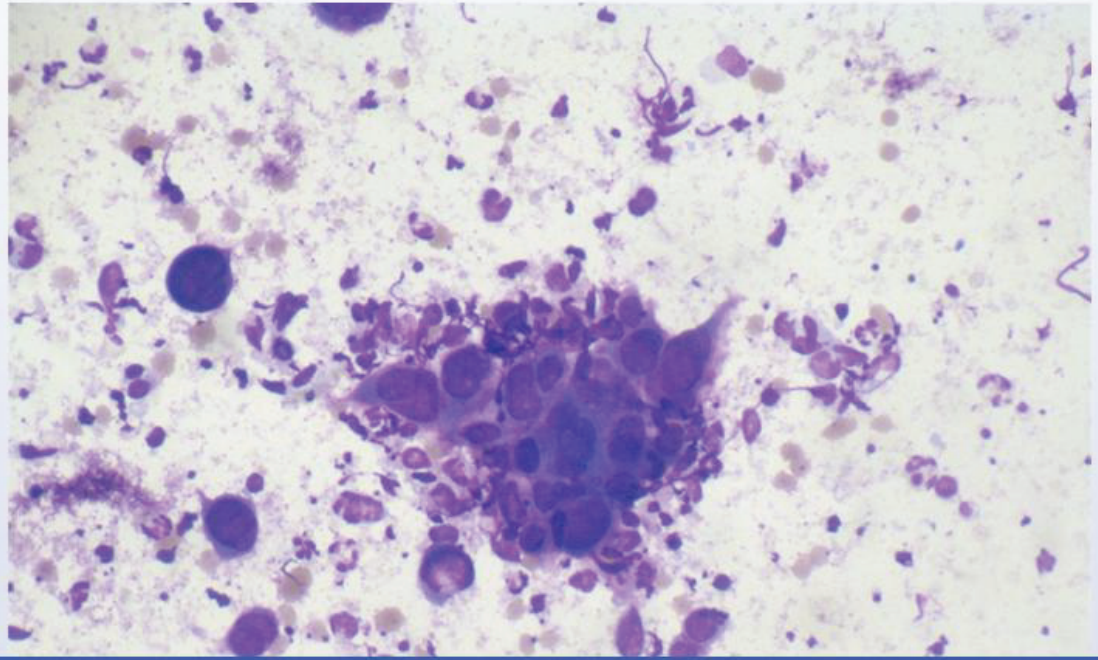
- HIV-1 envelope glycoprotein biosynthesis, trafficking, and incorporation

Pharmacology Infectious Diseases Antiretroviral therapy

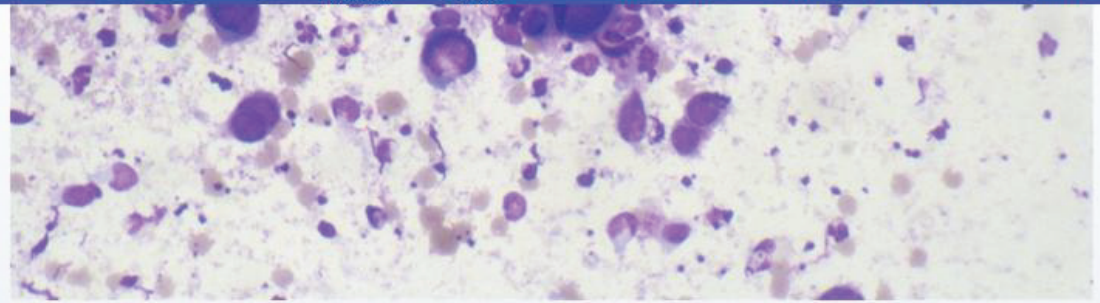
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A 23-year-old man comes to the office due to penile ulcers that appeared after unprotected sexual intercourse. Physical examination shows 3 subcentimeter ulcers on the penile shaft. Microscopic examination of a scraping from an ulcer base reveals the following:



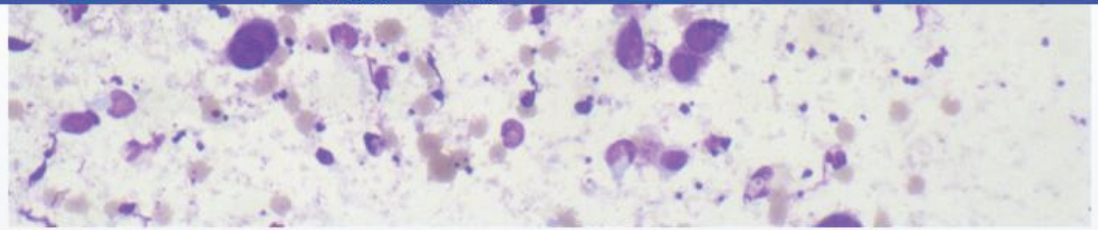
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Which of the following medications is most appropriate for this patient?

- A. Acyclovir
- B. Azithromycin
- C. Doxycycline
- D. Fluconazole
- E. Penicillin
- F. Permethrin

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Which of the following medications is most appropriate for this patient?

- A. Acyclovir (72%)
- B. Azithromycin (6%)
- C. Doxycycline (6%)
- D. Fluconazole (0%)
- E. Penicillin (12%)
- F. Permethrin (1%)

Correct

72%

29 secs

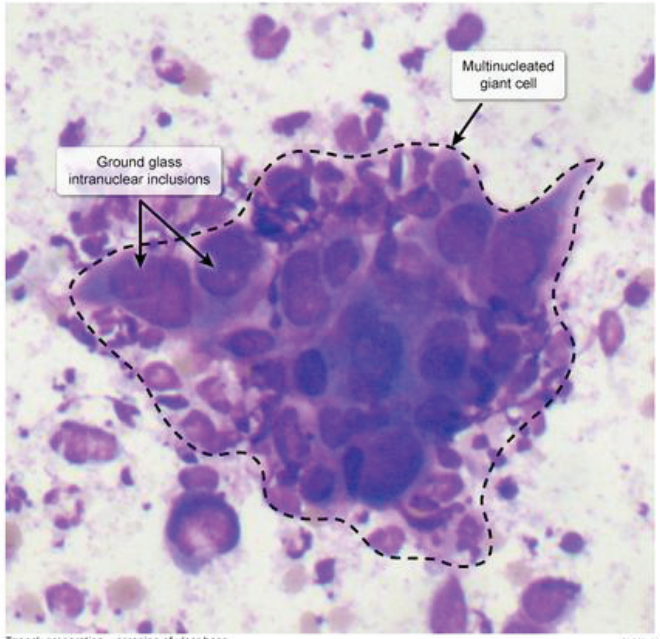
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Herpes simplex



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Tzanck preparation – scraping of ulcer base

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Microscopy of this patient's penis ulcer reveals a **multinucleated giant cell** with intracytoplasmic ground-glass opacities, raising strong suspicion for herpes simplex virus **(HSV) infection**. Genital HSV is usually caused by HSV type 2, which is spread primarily via direct skin contact with herpetic sores or infected genital secretions during sexual activity. Initial infection is often characterized by **painful genital ulcers**, fever, lymphadenopathy, and dysuria. Symptoms typically resolve within a few weeks, but latent infection develops in the dorsal root ganglia and can periodically reactivate, leading to recurrence.

HSV is generally diagnosed by cell culture or PCR, but **Tzanck smear** (as seen above) can reveal the cytopathic effects of the virus (eg, multinucleated giant cells, acantholytic cells, keratinocyte ballooning, nuclear molding). Oral antiviral agents such as **acyclovir**, a competitive inhibitor of viral DNA polymerase, help speed symptom resolution.

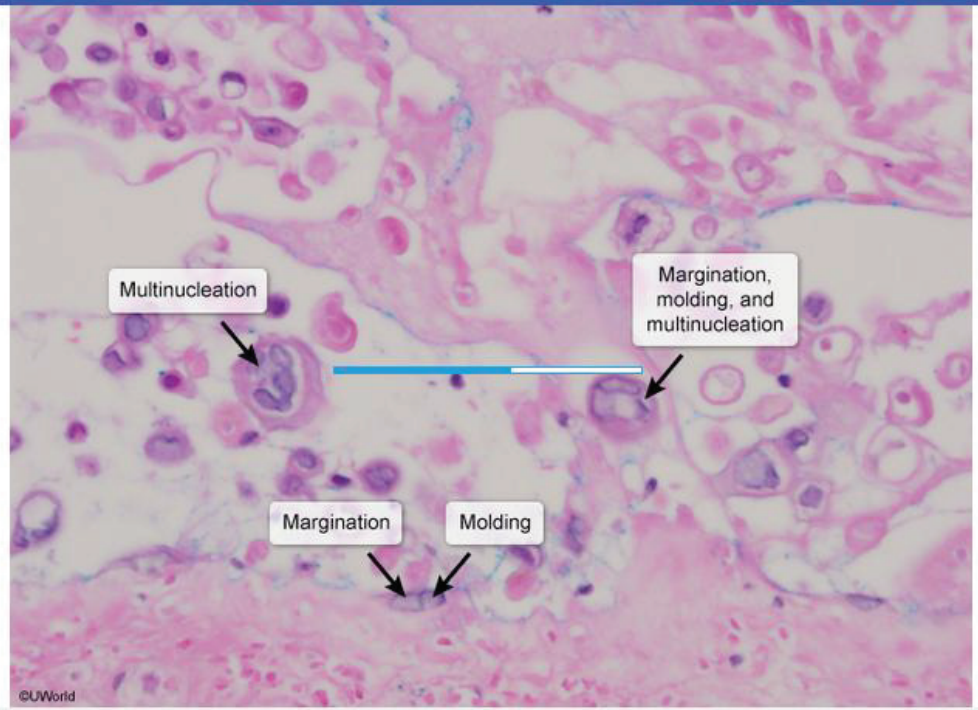
(Choice B) Azithromycin can be used to treat chancroid, which is characterized by the formation of a papule that evolves into a pustule and then an ulcer. However, it is very rare in the United States and is caused by the gram-negative organism *Haemophilus ducreyi*; multinucleated giant cells would not be seen.

(Choice C) Doxycycline can treat lymphogranuloma venereum, a genital infection caused by certain serotypes of *Chlamydia trachomatis*. This disease is marked by the formation of a small genital ulcer,

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(Choice C) Doxycycline can treat lymphogranuloma venereum, a genital infection caused by certain serotypes of *Chlamydia trachomatis*. This disease is marked by the formation of a small genital ulcer, followed by significant lymph node inflammation and pain in the inguinal or femoral region. *C trachomatis* appears as intravacuolar organisms in macrophages.

(Choice D) Fluconazole can treat *Candida balanitis*, which is typically marked by a painful, pruritic, erythematous rash. Yeasts and pseudohyphae can often be seen on microscopy.

(Choice E) Penicillin can be used to treat syphilis, a spirochetal infection caused by *Treponema pallidium* that begins with the formation of a chancre (painless ulcer with heaped-up borders and a clean base) at the site of inoculation. Diagnosis is generally made with serologic testing because *T pallidium* cannot be cultured; multiple ulcers and multinucleated giant cells are not typically seen.

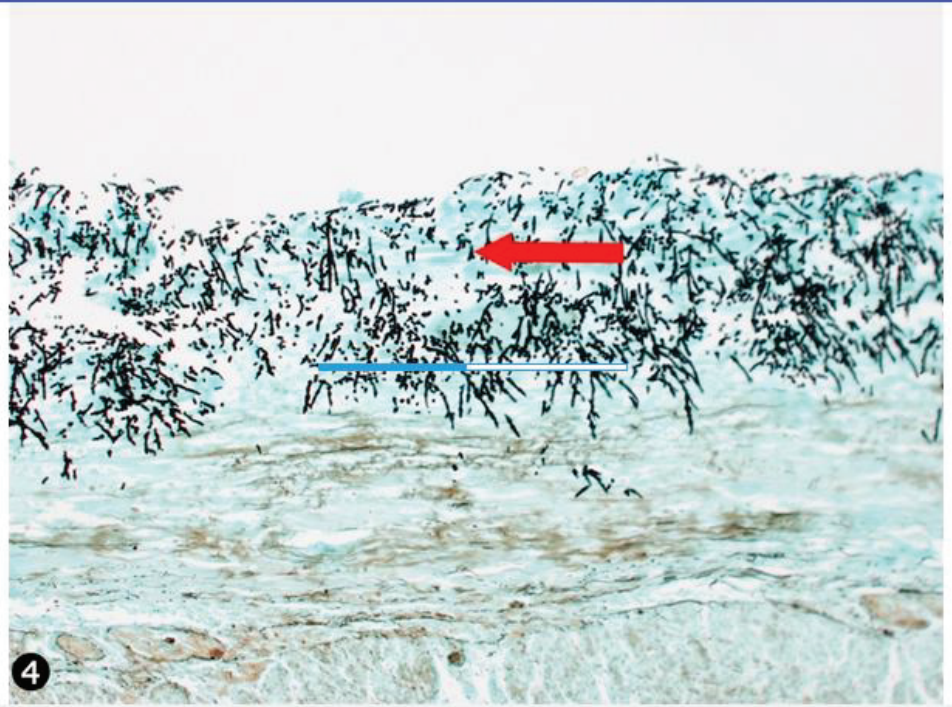
(Choice F) Permethrin can be used to treat pubic lice, which are associated with significant pruritus of hairy genital areas. Lice can generally be visualized on the hair shaft.

Educational objective:
Herpes simplex virus is a common, sexually transmitted infection marked by the formation of painful genital ulcers. Tzanck smear can reveal the characteristic cytopathic effects of the virus, including multinucleated

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appears as intravacuolar organisms in macrophages.

(Choice D) Fluconazole can treat *Candida balanitis*, which is typically marked by a painful, pruritic, erythematous rash. Yeasts and pseudohyphae can often be seen on microscopy.

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(Choice F) Permethrin can be used to treat pubic lice, which are associated with significant pruritus of hairy genital areas. Lice can generally be visualized on the hair shaft.

Educational objective:
Herpes simplex virus is a common, sexually transmitted infection marked by the formation of painful genital ulcers. Tzanck smear can reveal the characteristic cytopathic effects of the virus, including multinucleated giant cells, ground-glass opacities, acantholytic cells, keratinocyte ballooning, and nuclear molding.

Microbiology	Infectious Diseases	HSV infection
Subject	System	Topic

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A 26-year-old man is being evaluated for recurrent boils and skin abscesses. Anterior nares swab culture is performed to determine colonization by the culprit bacteria, which yields gram-positive cocci in clusters. The bacteria are able to grow in a media containing oxacillin. PCR testing reveals the pathogen has acquired the *mecA* gene. These bacteria are most likely to be resistant to which of the following antibiotics?

A. Cefazolin
B. Clindamycin
C. Doxycycline
D. Trimethoprim-sulfamethoxazole
E. Vancomycin

Submit

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A 26-year-old man is being evaluated for recurrent boils and skin abscesses. Anterior nares swab culture is performed to determine colonization by the culprit bacteria, which yields gram-positive cocci in clusters. The bacteria are able to grow in a media containing oxacillin. PCR testing reveals the pathogen has acquired the *mecA* gene. These bacteria are most likely to be resistant to which of the following antibiotics?

- A. Cefazolin (60%)
- B. Clindamycin (4%)
- C. Doxycycline (3%)
- D. Trimethoprim-sulfamethoxazole (1%)
- E. Vancomycin (29%)

Correct

60% Answered correctly

54 secs Time Spent

12/11/2020 Last Updated

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This patient with recurrent boils and skin abscesses is likely colonized with ***Staphylococcus aureus***, a gram-positive cocci that grows in clusters. Methicillin-resistant strains are able to grow in the presence of oxacillin due to the acquisition of a mobile genetic element that contains the ***mecA* gene**, which encodes for **penicillin-binding protein (PBP) 2a**. PBPs catalyze peptidoglycan cross-linking during cell wall synthesis; they are the target of beta-lactam medications, which bind to and irreversibly destroy the enzyme. Unlike other PBPs, PBP 2a has a **low affinity for beta-lactams** and continues to cross-link peptidoglycan in the presence of oxacillin, methicillin, cephalosporins (eg, **cefazolin**), and other beta-lactam medications.

Therefore, treatment of methicillin-resistant *S aureus* (MRSA) generally requires the use of a non–beta-lactam drug. Common medications for MRSA include trimethoprim-sulfamethoxazole (inhibits 2 steps in folate synthesis), clindamycin (inhibits bacterial protein synthesis by binding to the 50s ribosomal subunit), doxycycline (inhibits protein synthesis by binding to the 30s ribosomal subunit), or vancomycin (inhibits integration of peptidoglycan subunits) **(Choices B, C, D, and E)**.

Educational objective:

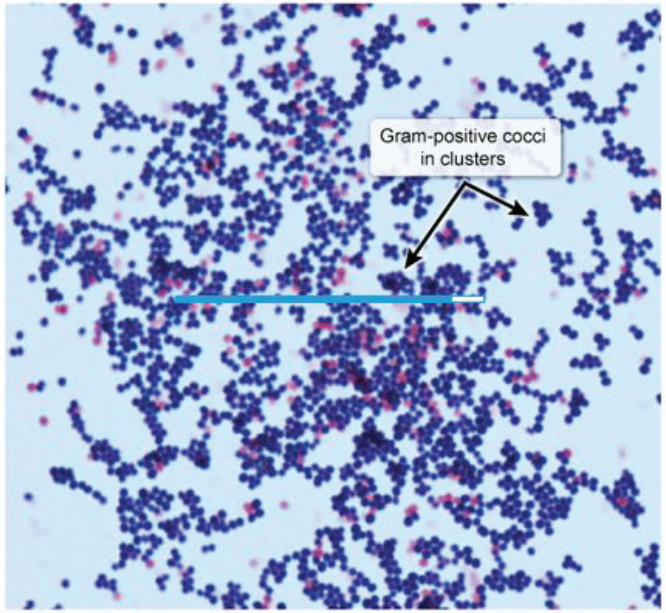
Methicillin-resistant *Staphylococcus aureus* (MRSA) is resistant to most beta-lactam medications (eg, oxacillin, methicillin, cephalosporins) due to the acquisition of a mobile genetic element that contains the

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Exhibit Display

Staphylococcus aureus



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oxacillin, methicillin, cephalosporins) due to the acquisition of a mobile genetic element that contains the

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enzyme. Unlike other PBPs, PBP 2a has a **low affinity for beta-lactams** and continues to cross-link peptidoglycan in the presence of oxacillin, methicillin, cephalosporins (eg, **cefazolin**), and other beta-lactam medications.

Therefore, treatment of methicillin-resistant *S aureus* (MRSA) generally requires the use of a non–beta-lactam drug. Common medications for MRSA include trimethoprim-sulfamethoxazole (inhibits 2 steps in folate synthesis), clindamycin (inhibits bacterial protein synthesis by binding to the 50s ribosomal subunit), doxycycline (inhibits protein synthesis by binding to the 30s ribosomal subunit), or vancomycin (inhibits integration of peptidoglycan subunits) **(Choices B, C, D, and E)**.

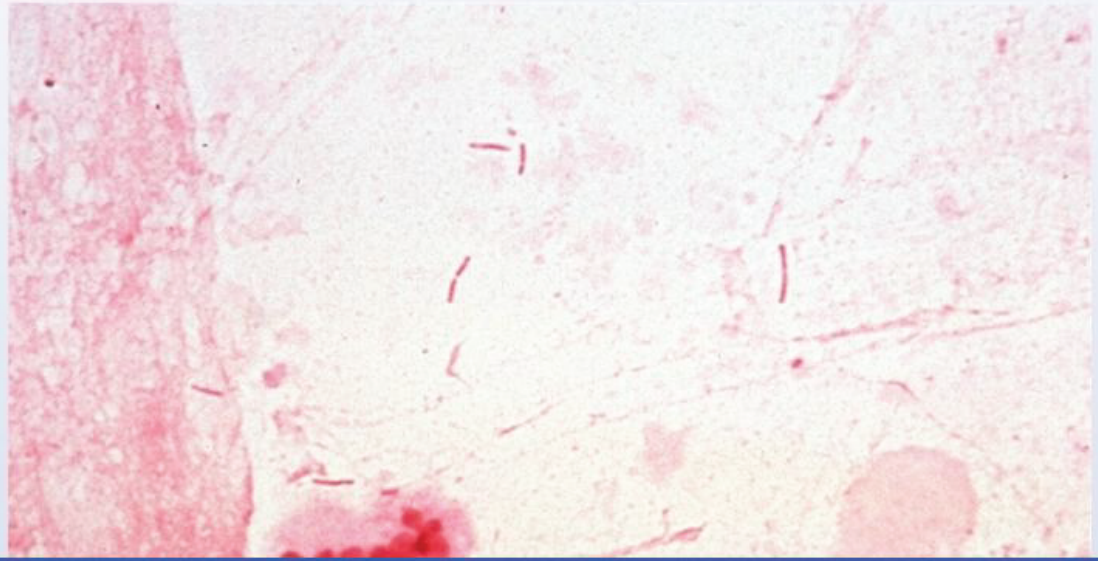
Educational objective:

Methicillin-resistant *Staphylococcus aureus* (MRSA) is resistant to most beta-lactam medications (eg, oxacillin, methicillin, cephalosporins) due to the acquisition of a mobile genetic element that contains the *mecA* gene. This gene encodes for a specialized penicillin-binding protein that has low affinity for beta-lactam antibiotics. Treatment of MRSA therefore requires a non–beta-lactam medication such as trimethoprim-sulfamethoxazole, clindamycin, doxycycline, or vancomycin.

Pharmacology	Infectious Diseases	Antibiotic resistance
Subject	System	Topic

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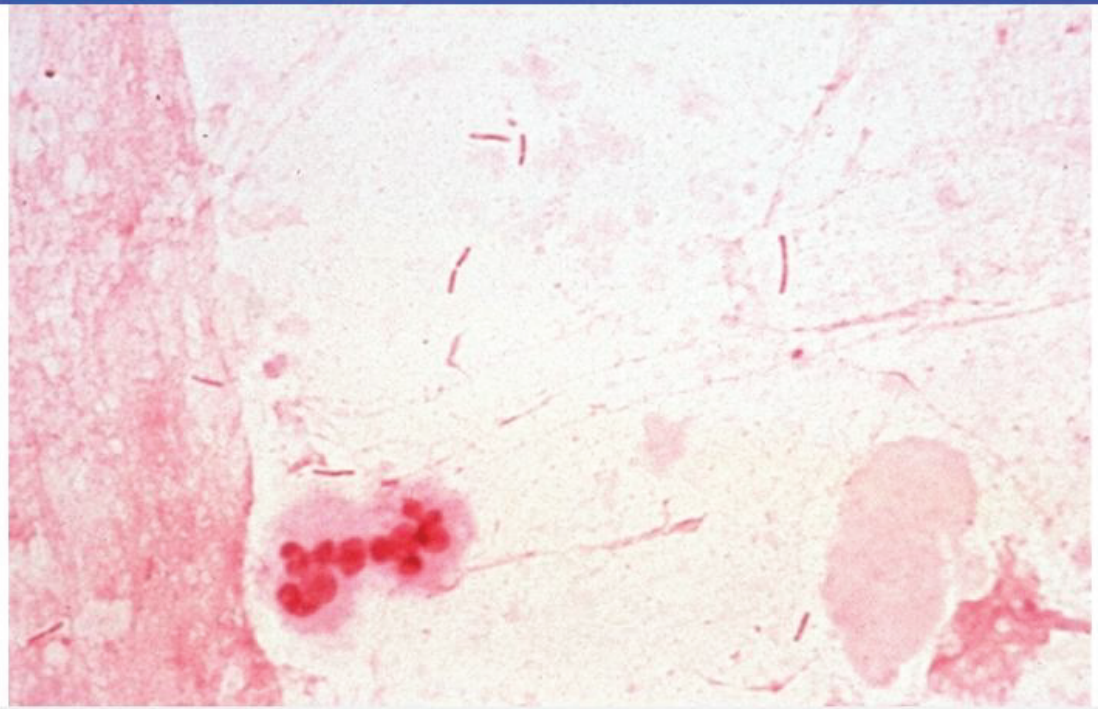
A 65-year-old man is admitted to the intensive care unit with second- and third-degree burns over 25% of his total body surface area. Intravenous fluids and analgesics are administered, and his wounds are cleaned and debrided. After 7 days, the patient develops a fever and his leukocyte count rises to 16,000 cells/μL. Examination of the burns on his left leg shows surrounding warmth, erythema, and induration. Gram stain of his wound tissue is shown in the image below.



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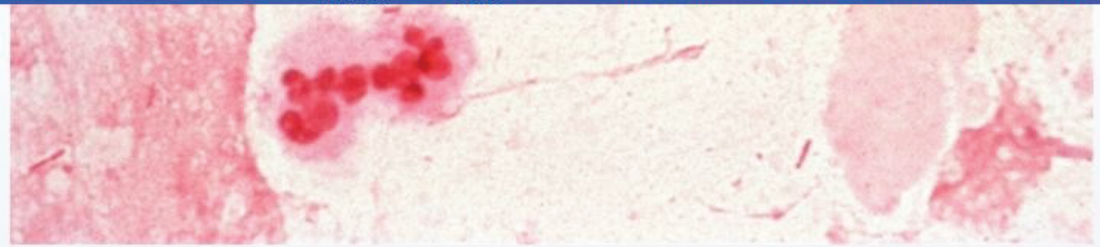
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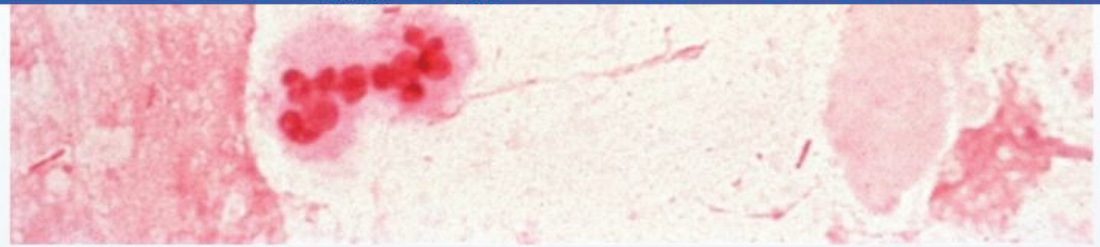


Culture on MacConkey agar grows oxidase-positive colonies that do not ferment lactose. Which of the following is the best initial treatment for this patient?

- A. Cefepime
- B. Ceftriaxone
- C. Doxycycline
- D. Moxifloxacin
- E. Trimethoprim-sulfamethoxazole

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Culture on MacConkey agar grows oxidase-positive colonies that do not ferment lactose. Which of the following is the best initial treatment for this patient?

- A. Cefepime (45%)
- B. Ceftriaxone (23%)
- C. Doxycycline (7%)
- D. Moxifloxacin (15%)
- E. Trimethoprim-sulfamethoxazole (8%)

Correct

45%

58 secs

03/10/2021

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Antibiotics effective against *Pseudomonas aeruginosa*

Class	Drugs
Anti-pseudomonal penicillins	• Ticarcillin • Piperacillin
Cephalosporins	• Ceftazidime (3rd generation) • Cefepime (4th generation)
Aminoglycosides	• Amikacin • Gentamicin • Tobramycin
Fluoroquinolones	• Ciprofloxacin • Levofloxacin
Monobactams	• Aztreonam
Carbapenems	• Imipenem • Meropenem

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Burn patients are at increased risk of bacterial infection due to loss of the barrier function of the skin, post-burn immune dysfunction, and lack of blood flow to necrotic areas. Common pathogens include Gram-positive (eg, *Staphylococcus aureus*, *Enterococcus* species) and Gram-negative (eg, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Acinetobacter* species) bacteria.

This patient's burn is infected with Gram-negative rods that are oxidase-positive and non-lactose-fermenting, making *P aeruginosa* the most likely pathogen. Cephalosporins such as cefepime and ceftazidime have good anti-pseudomonal coverage.

(Choice B) Ceftriaxone is a third-generation cephalosporin used primarily for the treatment of community-acquired pneumonia and bacterial meningitis. It has activity against some Gram-positive (eg, *Streptococcus pneumoniae*, *S pyogenes*) and Gram-negative (eg, *Haemophilus influenzae, K pneumoniae*, *E coli*) pathogens. Unlike ceftazidime, it has poor activity against *P aeruginosa.*

(Choice C) Doxycycline is effective against Lyme disease and many tickborne rickettsial diseases but does not have good anti-pseudomonal coverage.

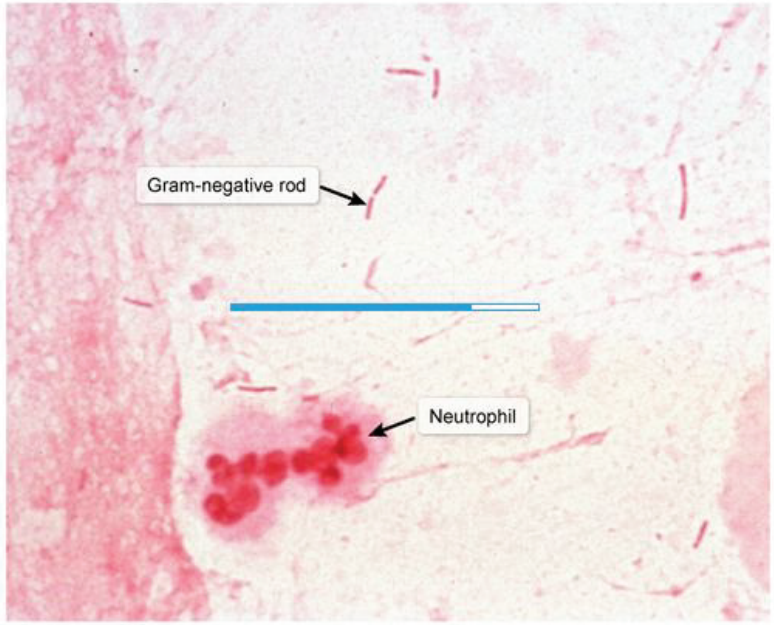
(Choice D) Moxifloxacin is a fluoroquinolone used mainly for the treatment of bacterial infections that cause exacerbation of chronic obstructive pulmonary disease, sinusitis, and community-acquired pneumonia. Unlike ciprofloxacin and levofloxacin, moxifloxacin has poor anti-pseudomonal activity.

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Exhibit Display

Pseudomonas aeruginosa



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(Choice C) Doxycycline is effective against Lyme disease and many tickborne rickettsial diseases but does not have good anti-pseudomonal coverage.

(Choice D) Moxifloxacin is a fluoroquinolone used mainly for the treatment of bacterial infections that cause exacerbation of chronic obstructive pulmonary disease, sinusitis, and community-acquired pneumonia. Unlike ciprofloxacin and levofloxacin, moxifloxacin has poor anti-pseudomonal activity.

(Choice E) Trimethoprim-sulfamethoxazole is used to treat susceptible organisms that cause urinary tract, gastrointestinal, and skin infections. It is the drug of choice for organisms such as *Pneumocystis jiroveci, Toxoplasma gondii, Nocardia,* and *Stenotrophomonas maltophilia*. It does not have activity against *P aeruginosa*.

Educational objective:

Pseudomonas aeruginosa is a major pathogen in burn patients. Only a few specific penicillins (eg, ticarcillin, piperacillin) and cephalosporins (eg, ceftazidime, cefepime) have activity against it. Certain aminoglycosides, fluoroquinolones (eg, ciprofloxacin, levofloxacin), and carbapenems (eg, imipenem, meropenem) are also effective.

References

- Update on the treatment of Pseudomonas aeruginosa pneumonia.

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order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

A 29-year-old woman is brought to the emergency department with new-onset generalized tonic-clonic seizures. She has a history of HIV and has not been taking her medications consistently. According to her family, she has been sleepy and weak for the past 2 weeks. She has not had much of an appetite and has recently spent most of her time in bed. MRI of the head demonstrates 2 ring-enhancing focal lesions with surrounding edema in the right frontal lobe.

Item 1 of 2

Which of the following would be effective against the pathogen most likely responsible for this patient's symptoms?

A. Amphotericin B
B. Ampicillin
C. Ganciclovir
D. Isoniazid and rifampin
E. Pyrimethamine and sulfadiazine

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A 29-year-old woman is brought to the emergency department with new-onset generalized tonic-clonic seizures. She has a history of HIV and has not been taking her medications consistently. According to her family, she has been sleepy and weak for the past 2 weeks. She has not had much of an appetite and has recently spent most of her time in bed. MRI of the head demonstrates 2 ring-enhancing focal lesions with surrounding edema in the right frontal lobe.

Item 1 of 2

Which of the following would be effective against the pathogen most likely responsible for this patient's symptoms?

- A. ~~Amphotericin B~~ (24%)
- B. ~~Ampicillin~~ (1%)
- C. ~~Ganciclovir~~ (7%)
- D. Isoniazid and rifampin (2%)
- ✓ E. Pyrimethamine and sulfadiazine (63%)

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Toxoplasma gondii is an obligate intracellular protozoan with a worldwide distribution. The cat is the definitive host of this protozoan, with humans infected following ingestion of food or water contaminated with cat feces (containing oocysts) or undercooked meat (containing pseudocysts). Immunocompromised individuals exposed to *T gondii* can develop encephalitis with multiple necrotizing brain lesions, resulting in fever, headache, altered mental status, and focal neurologic findings. In this patient with **HIV** who has **seizures** and **multiple ring-enhancing lesions** with mass effect, **cerebral toxoplasmosis** is a likely diagnosis. First-line treatment (which can be given empirically, particularly if test results are unrevealing) includes a combination of **pyrimethamine and sulfadiazine** (or pyrimethamine and clindamycin in case of sulfa drug hypersensitivity) along with leucovorin (folinic acid).

(Choice A) Amphotericin (with flucytosine) is used to treat cryptococcal meningitis, a well-known cause of meningitis in AIDS patients that typically manifests with nausea, vomiting, nuchal rigidity, and altered mental status. Ring-enhancing lesions are not commonly seen on imaging as cryptococcomas are rare. Amphotericin can treat invasive aspergillosis; however, central nervous system aspergillosis more classically presents as an abscess (eg, single ring-enhancing lesion), is often accompanied by pulmonary (eg, cough, dyspnea) and orbital manifestations in patients with HIV, and is primarily treated with voriconazole rather than amphotericin.

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classically presents as an abscess (eg, single ring-enhancing lesion), is often accompanied by pulmonary (eg, cough, dyspnea) and orbital manifestations in patients with HIV, and is primarily treated with voriconazole rather than amphotericin.

(Choice B) Ampicillin is typically used to treat *Listeria* infection. *L monocytogenes* can cause meningitis in immunosuppressed patients but does not typically form ring-enhancing lesions.

(Choice C) Ganciclovir is used in the treatment of cytomegalovirus (CMV) infection. CMV primarily causes symptomatic disease (eg, retinitis, esophagitis, pneumonia) in the immunosuppressed. Characteristic manifestations of central nervous system involvement include polyneuropathy, transverse myelitis, and encephalitis.

(Choice D) In developing countries, mycobacterial infection causes brain tuberculomas (nodular granulomatous lesions), but this would be less likely in the United States. Tuberculoma treatment typically includes 5 antitubercular drugs rather than only isoniazid and rifampin.

The differential diagnosis for this patient also includes primary central nervous system lymphoma (second most common after cerebral toxoplasmosis), primary brain tumors (eg, glioblastoma multiforme), metastatic carcinoma, and fungal or bacterial abscesses.

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Characteristic manifestations of central nervous system involvement include polyneuropathy, transverse myelitis, and encephalitis.

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The differential diagnosis for this patient also includes primary central nervous system lymphoma (second most common after cerebral toxoplasmosis), primary brain tumors (eg, glioblastoma multiforme), metastatic carcinoma, and fungal or bacterial abscesses.

Educational objective:
In patients with HIV, the presence of multiple ring-enhancing lesions with mass effect is most often indicative of toxoplasmosis, followed by primary central nervous system lymphoma.

References

- Use of CT and MR imaging to distinguish intracranial lesions and to define the need for biopsy in AIDS patients.

Microbiology	Infectious Diseases	Toxoplasmosis
Subject	System	Topic

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Item 2 of 2

After 10 days of empiric therapy, the patient's clinical situation has not improved significantly and the appearance of the brain lesions on MRI is unchanged. Results for *Toxoplasma* serology and polymerase chain reaction (PCR) testing are negative. Cerebrospinal fluid PCR analysis for Epstein-Barr virus is positive. Tissue biopsy from the frontal lobe lesions would likely predominantly show an abnormal population of which of the following cells?

- A. B-lymphocytes
- B. Eosinophils
- C. Macrophages
- D. Oligodendrocytes
- E. T-lymphocytes

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Item 2 of 2

After 10 days of empiric therapy, the patient's clinical situation has not improved significantly and the appearance of the brain lesions on MRI is unchanged. Results for *Toxoplasma* serology and polymerase chain reaction (PCR) testing are negative. Cerebrospinal fluid PCR analysis for Epstein-Barr virus is positive. Tissue biopsy from the frontal lobe lesions would likely predominantly show an abnormal population of which of the following cells?

- ✓ A. B-lymphocytes (61%)
- B. ~~Eosinophils~~ (1%)
- C. Macrophages (4%)
- D. ~~Oligodendrocytes~~ (2%)
- E. T-lymphocytes (30%)

Correct

61%
Answered correctly

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In a patient with HIV and multiple ring-enhancing lesions being treated empirically for toxoplasmosis, lack of a clinical or imaging response after 1-3 weeks of therapy should raise suspicion for other conditions requiring further evaluation, especially given negative *Toxoplasma* serologies. **Primary central nervous system lymphoma** (PCNSL) is the second most common cause of ring-enhancing lesions with mass effect in HIV. Classically, large, solitary lesions are more likely to suggest PCNSL rather than toxoplasmosis; however, multiple lesions (as seen in this patient) are also common in PCNSL.

PCNSL is a diffuse, large-cell non-Hodgkin lymphoma of **B-cell origin** that usually occurs as a late complication of HIV infection. **Epstein-Barr virus** (EBV) is identified in almost all cases. Diagnosis of PCNSL can be made by positive EBV polymerase chain reaction analysis in the cerebrospinal fluid. Definitive diagnosis requires brain biopsy. Although EBV infections in general can be associated with abnormal T-lymphocytes (eg, atypical lymphocytes), T cell infiltration is not commonly seen on brain tissue biopsy of patients with HIV who have PCNSL. T-lymphocytes are the malignant cells in AIDS-associated T-cell lymphoma, not PCNSL **(Choice E)**.

(Choice B) Eosinophils do not give rise to solid tumors.

(Choice C) Macrophages are the primary cell population in histiocytomas. Patients with Langerhans cell histiocytosis may develop eosinophilic granulomas that preferentially affect the skull, but ring-enhancing

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T-cell lymphoma, not PCNSL **(Choice E)**.

(Choice B) Eosinophils do not give rise to solid tumors.

(Choice C) Macrophages are the primary cell population in histiocytomas. Patients with Langerhans cell histiocytosis may develop eosinophilic granulomas that preferentially affect the skull, but ring-enhancing lesions are not seen.

(Choice D) Oligodendrocytes can form oligodendrogliomas. Astrocytes are the precursor cells for glioblastoma multiforme, which can present with a ring-enhancing lesion.

Educational objective:
Primary central nervous system lymphoma is typically composed of B-lymphocytes.

References

- Epstein-Barr virus in AIDS-related primary central nervous system lymphoma.
- T-cell infiltration of primary CNS lymphoma.

Microbiology	Infectious Diseases	Cns lymphoma
Subject	System	Topic

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An unvaccinated 20-month-old girl is brought to the emergency department with a rash. Three days ago, she developed a fever along with cough, congestion, and red eyes. The rash appeared on her face yesterday and spread to her trunk, arms, and legs today. The patient's temperature is 39.4 C (103 F). She is lethargic and ill appearing. Physical examination shows conjunctival injection and a diffuse, maculopapular, erythematous rash. She is admitted to the hospital for further management. Deficiency of which of the following is associated with a high rate of complications from this patient's condition?

A. Vitamin A
B. Vitamin B_6
C. Vitamin B_{12}
D. Vitamin D
E. Vitamin E
F. Vitamin K

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- A. Vitamin A (63%)
- B. Vitamin B_6 (9%)
- C. Vitamin B_{12} (4%)
- D. Vitamin D (1%)
- E. Vitamin E (6%)
- F. Vitamin K (13%)

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Measles virus (rubeola)	
Clinical presentation	• Prodrome (eg, cough, coryza, conjunctivitis, fever, Koplik spots) • Maculopapular exanthem ○ Cephalocaudal & centrifugal spread ○ Spares palms/soles
Complications	• Primary measles pneumonia • Secondary bacterial infections (pneumonia & otitis media) • Neurologic ○ Encephalitis (within days) ○ Acute disseminated encephalomyelitis (within weeks) ○ Subacute sclerosing panencephalitis (within years)
Prevention	• Live attenuated measles vaccine

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This patient's history of fever, cough, congestion, and conjunctivitis followed by a maculopapular rash is consistent with measles. **Measles** is a highly contagious paramyxovirus that spreads by contact or aerosolized respiratory droplets. This vaccine-preventable infection can be life-threatening. The classic exanthema starts on the face and spreads in a cephalocaudal and centrifugal pattern. Erythematous, blanching, maculopapular lesions often progress to a deep red or brown, nonblanching, coalesced rash.

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such as rickets and osteomalacia. Vitamin E deficiency results in hemolytic anemia and neurologic

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Vitamin A supplementation is recommended, especially in patients with vitamin A deficiency. Acute measles infection depletes vitamin A stores, resulting in a risk of keratitis and corneal ulceration. Vitamin A helps **prevent** and treat these **ocular complications**. In addition, it **reduces** risk of other comorbidities (eg, pneumonia, encephalitis), **recovery time**, and **length of hospital stay**. No other vitamin is linked to measles.

(Choice B) Vitamin B_6, or pyridoxine, deficiency can result in oral abnormalities (eg, stomatitis, cheilosis) and irritability. Vitamin B_6 is given therapeutically in specific circumstances (eg, to decrease adverse side effects of isoniazid therapy, to decrease homocysteine levels).

(Choice C) Deficiency of vitamin B_{12}, or cobalamin, results in macrocytic anemia; hypersegmented neutrophils on peripheral smear; and neurologic signs, such as paresthesias. Patients with a vegan diet are at risk as this vitamin is only found in animal products.

(Choices D, E, and F) Like vitamin A, vitamins D, E, and K are fat-soluble vitamins and often present in patients with fat malabsorption (eg, cystic fibrosis). Vitamin D deficiency results in bony abnormalities, such as rickets and osteomalacia. Vitamin E deficiency results in hemolytic anemia and neurologic abnormalities (eg, ataxia). Vitamin K deficiency presents with easy bleeding (eg, easy bruising, gum bleeding, hematuria, hematochezia).

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effects of isoniazid therapy, to decrease homocysteine levels).

(Choice C) Deficiency of vitamin B_{12}, or cobalamin, results in macrocytic anemia; hypersegmented neutrophils on peripheral smear; and neurologic signs, such as paresthesias. Patients with a vegan diet are at risk as this vitamin is only found in animal products.

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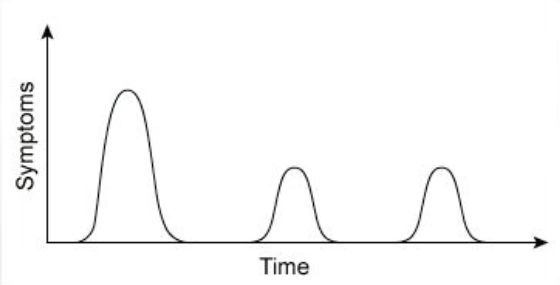
Educational objective:
Vitamin A can be beneficial in the treatment of measles infection by reducing comorbidities (eg, ocular complications, diarrhea, pneumonia), recovery time, and length of hospital stay.

References

- Vitamin A for treating measles in children.
- Use of combination measles, mumps, rubella, and varicella vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP).

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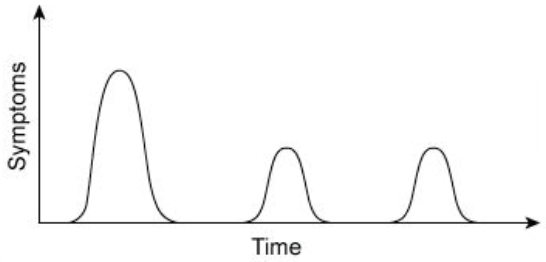
A 23-year-old woman diagnosed with a viral infection participates in a longitudinal research study. The patient experiences symptoms of similar spectrum over a specific time, as shown in the image.



Which of the following mechanisms is most likely responsible for the pattern of illness seen in this patient?

A. Latent infection within hepatocytes
B. Latent infection within neuronal cell bodies
C. Latent infection within transformed B-lymphocytes
D. Superinfection by a different virus
E. Viral surface protein changes from gene reassortment

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Which of the following mechanisms is most likely responsible for the pattern of illness seen in this patient?

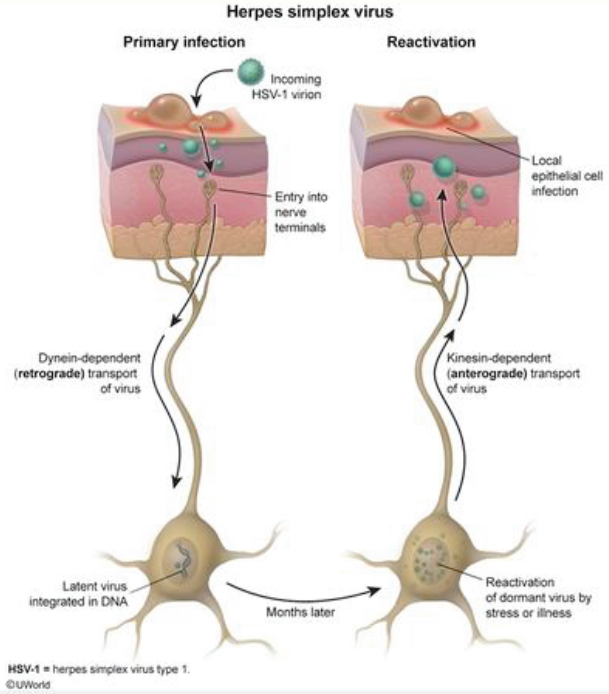
A. Latent infection within hepatocytes (17%)
B. Latent infection within neuronal cell bodies (55%)
C. Latent infection within transformed B-lymphocytes (8%)
D. Superinfection by a different virus (1%)
E. Viral surface protein changes from gene reassortment (17%)

Correct
55%
56 secs
03/01/2021

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HSV-1 = herpes simplex virus type 1.
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Patients with **herpes simplex virus** (HSV) usually have symptoms that flare and remit in a cyclical fashion. Initial HSV infections are marked by viral replication at the site of exposure (eg, perioral or genital skin), which leads to vesicular mucocutaneous lesions and flulike symptoms. Manifestations last a week or two and then resolve spontaneously when viral replication ceases. However, the virus also spreads to dermal nerve terminals and is transported in a retrograde fashion to the **sensory ganglia**, where it establishes a lifelong **latent infection** within the **neuronal cell bodies**.

During latent infection, no viral replication occurs, so the disease is asymptomatic. However, infected cells continue to produce some HSV genes (eg, latency-associated transcript gene), and stress and other triggers can reactivate viral replication and lead to the re-emergence of symptoms (eg, vesicular lesions on the oral/genital mucous membranes, low-grade fever, malaise). Recurrent symptoms last a week or two and then resolve; they are often less severe than the initial episode.

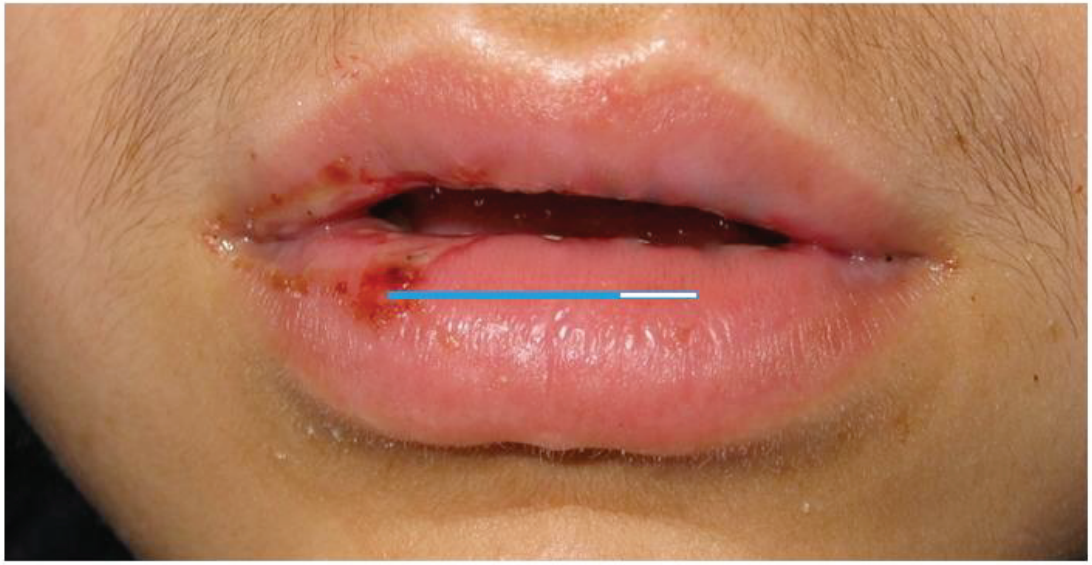
(Choice A) Infection with hepatitis B or C virus usually results in chronic hepatocyte infection and persistent viral replication. Patients are usually asymptomatic for years or decades and then eventually develop cirrhosis and related complications (eg, jaundice, ascites, encephalopathy). Latent infections do not occur.

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HSV-1 = herpes simplex virus type 1.

Exhibit Display



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(Choice C) Epstein-Barr virus has a tropism for B-lymphocytes. Initial infection is associated with infectious mononucleosis (eg, sore throat, lymphadenopathy, malaise, atypical lymphocytosis); latent infection is usually asymptomatic, but there is a small risk of B-cell or Hodgkin lymphoma due to malignant transformation. Both Epstein-Barr virus and herpes simplex virus are members of the Herpesviridae family.

(Choice D) Hepatitis D virus is a small RNA molecule that requires coinfection with hepatitis B virus to have complete viral assembly. Superinfection by hepatitis D virus in patients with hepatitis B virus can lead to acute hepatic failure.

(Choice E) Influenza has a segmented genome, which leads to high rates of gene reassortment when 2 strains infect the same cell. Gene reassortment of surface glycoproteins (eg, hemagglutinin, neuraminidase) causes new strains to emerge and can result in new infections in those with a history of previous influenza infection; because surface proteins have changed, previous immunity is insufficient.

Educational objective:
Patients infected with herpes simplex virus develop a lifelong latent infection of the sensory ganglion. Periodic viral replication can lead to symptoms that flare and resolve over time.

Microbiology Infectious Diseases HSV infection

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Viruses that cause latent infection	
Site of latency	**Virus**
Sensory neurons	Herpes simplex & varicella zoster viruses
B lymphocytes	Epstein-Barr virus
Myeloid cells	Cytomegalovirus, human herpesvirus 6 & 7
CD4 T lymphocytes	Human immunodeficiency virus
Stratified squamous epithelial cells	Human papilloma virus
Renal tubular epithelial cells	BK virus
Neuroglial cells	JC virus

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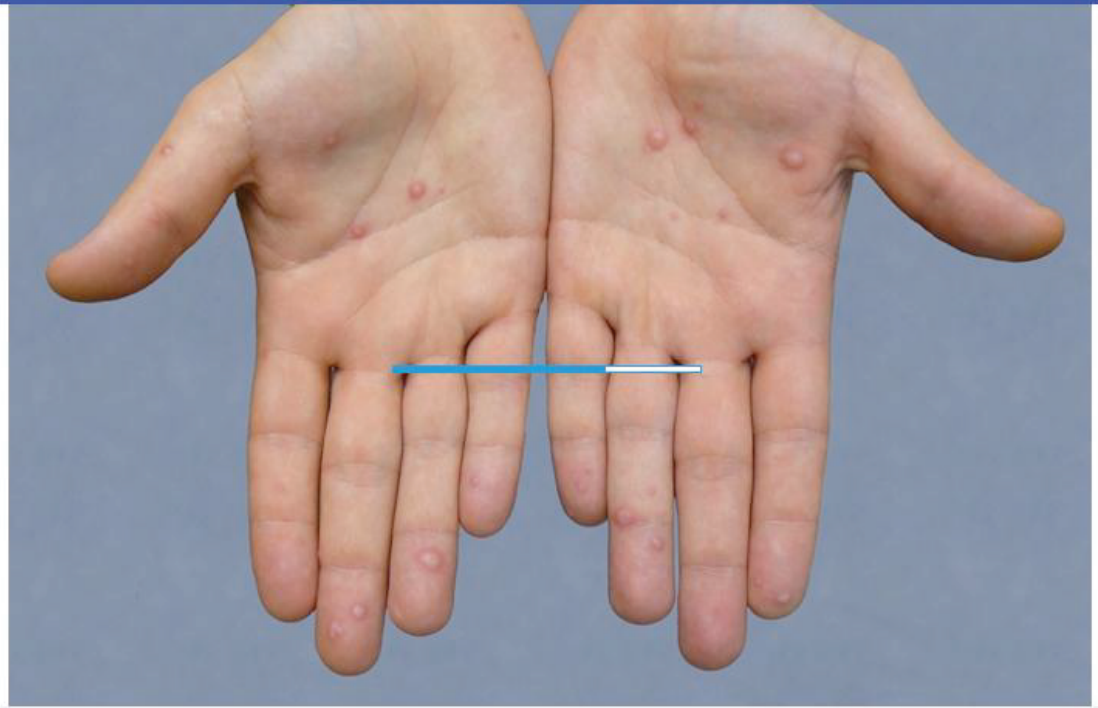
A 9-year-old boy is brought to the office due to throat pain and rash. Two days ago, the patient was sent home early from summer camp because of fever, sore throat, pain with eating, and rash on his extremities. He has no prior medical conditions and is up to date on immunizations. Temperature is 37.2 C (99 F); vital signs are otherwise normal. On physical examination, the conjunctivae are normal, and the tympanic membranes are clear. Several superficial ulcers are present on the buccal mucosa and soft palate; the tonsils appear normal and do not have exudate. Skin examination findings are shown in the exhibit. The infectious agent most likely responsible for this patient's current condition is also associated with which of the following?

A. Facial nerve palsy
B. Keratitis
C. Myocarditis
D. Symmetric polyarthritis
E. Temporal lobe encephalitis

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home early from summer camp because of fever, sore throat, pain with eating, and rash on his extremities. He has no prior medical conditions and is up to date on immunizations. Temperature is 37.2 C (99 F); vital signs are otherwise normal. On physical examination, the conjunctivae are normal, and the tympanic membranes are clear. Several superficial ulcers are present on the buccal mucosa and soft palate; the tonsils appear normal and do not have exudate. Skin examination findings are shown in the exhibit. The infectious agent most likely responsible for this patient's current condition is also associated with which of the following?

A. Facial nerve palsy (6%)
B. Keratitis (6%)
C. Myocarditis (55%)
D. Symmetric polyarthritis (11%)
E. Temporal lobe encephalitis (19%)

Correct
55%
38 secs
02/09/2021

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Enterovirus	
Epidemiology	• Infants & young children • Summer season • Fecal-oral transmission
Clinical features	• Herpangina (oral ulcerations) • Hand-foot-and-mouth disease (oral & extremity ulcerations) • Aseptic meningitis • Myocarditis

This patient has mouth ulcers and vesicular lesions on his hands, raising strong suspicion for **hand-foot-and-mouth disease** (HFMD). HFMD is caused by several different species of ***Enterovirus*** (*Picornaviridae* family), most often coxsackievirus A or Human enterovirus A. Most cases are transmitted by the fecal-oral route, and **outbreaks** often occur in communal settings (eg, day care, summer camp, schools) during the summer or early autumn; **children** age <7 are primarily affected.

The 2 most common presentations of enterovirus infection are:

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The 2 most common presentations of enterovirus infection are:

- **HFMD**, which is marked by low-grade fever, **oral enanthem** (vesicles/ulcers) on the tongue and buccal mucosa, and macular/**vesicular exanthem** on the **hands**, **feet**, buttocks, legs, and/or arms
- herpangina, which is characterized by high fever, oral ulcers, and no skin findings

Patients with enterovirus infection usually have self-limited disease. However, significant viremia occurs prior to the development of protective antibodies. Although generally asymptomatic and not associated with morbidity, a small minority of patients develop serious **myocarditis** (eg, congestive heart failure) or **CNS disease** (eg, aseptic meningitis).

(Choice A) Facial nerve palsy (Bell palsy) is associated with Lyme disease, which usually presents with a classic bull's-eye rash (erythema migrans) rather than ulcerative enanthem/exanthem.

(Choices B and E) Keratitis (cornea infection) and temporal lobe encephalitis are serious complications of herpes simplex virus (HSV). HSV gingivostomatitis presents with vesicles on the anterior oral mucosa, particularly the lips. Patients may also have concomitant herpetic whitlow, which usually appears as clusters of vesicles on the fingers (not diffuse blisters on the palm). *Enterovirus* is not associated with keratitis, and although it can cause CNS infection, temporal lobe encephalitis is more specific for HSV.

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The 2 most common presentations of enterovirus infection are:

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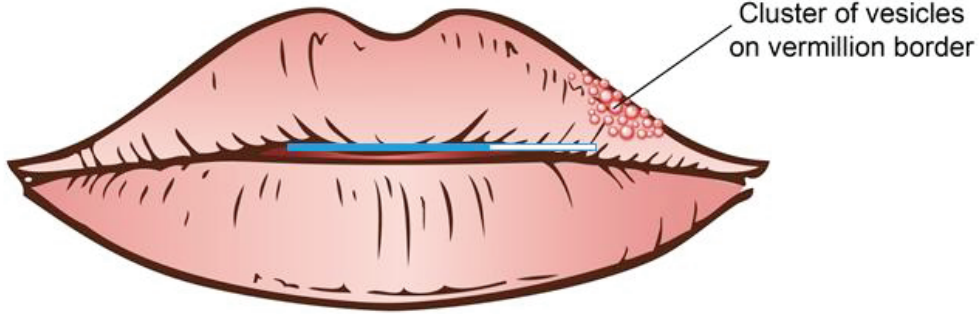
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The 2 most common presentations of enterovirus infection are:

Exhibit Display

Herpes simplex virus ("cold sore")



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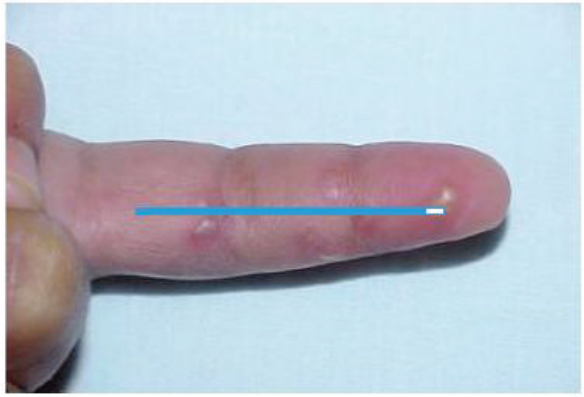
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The 2 most common presentations of enterovirus infection are:

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herpes simplex virus (HSV). HSV gingivostomatitis presents with vesicles on the anterior oral mucosa, particularly the lips. Patients may also have concomitant herpetic whitlow, which usually appears as clusters of vesicles on the fingers (not diffuse blisters on the palm). *Enterovirus* is not associated with keratitis, and although it can cause CNS infection, temporal lobe encephalitis is more specific for HSV.

(Choice D) Parvovirus B19 infection can cause a classic "slapped-cheek" rash (fifth disease) or a diffuse, reticulated rash. In some cases, particularly in adolescent girls or adult women, the infection is followed 1-2 weeks later by polyarthralgia or polyarthritis. *Enterovirus* does not usually cause joint manifestations.

Educational objective:

Hand-foot-and-mouth disease (oral ulceration and extremity rash) and herpangina (oral ulcerations without rash) are the most common manifestations of enteroviral infection. Rare but serious complications of infection include myocarditis and central nervous system disease (eg, aseptic meningitis).

References

- Tissue tropism, pathology and pathogenesis of enterovirus infection.
- The seasonality of nonpolio enteroviruses in the United States: patterns and drivers.

Microbiology Infectious Diseases Hand, foot, mouth disease

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www.ncbi.nlm.nih.gov/pubmed/29507246

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A group of researchers is investigating the causative agents responsible for infections in immunocompromised individuals. Patients with solid-organ malignancy who have received conventional chemotherapy are enrolled in the study. Detailed microbiologic data are obtained on any patient who develops fever during chemotherapy-induced neutropenia. Which of the following types of pathogens are most likely to be obtained in the majority of these patients?

A. Environmental, opportunistic pathogens
B. Hospital-acquired, drug-resistant bacteria
C. Pathogens spread from infected contacts
D. Patient's own endogenous bacterial flora
E. Previously latent, reactivated pathogens

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A group of researchers is investigating the causative agents responsible for infections in immunocompromised individuals. Patients with solid-organ malignancy who have received conventional chemotherapy are enrolled in the study. Detailed microbiologic data are obtained on any patient who develops fever during chemotherapy-induced neutropenia. Which of the following types of pathogens are most likely to be obtained in the majority of these patients?

A. ~~Environmental, opportunistic pathogens~~ (50%)
B. Hospital-acquired, drug-resistant bacteria (7%)
C. ~~Pathogens spread from infected contacts~~ (5%)
✓ D. Patient's own endogenous bacterial flora (25%)
E. ~~Previously latent, reactivated pathogens~~ (10%)

Correct

25%
Answered correctly

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Time Spent

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Last Updated

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Systemic chemotherapy targets rapidly dividing cancer cells but often incidentally damages other rapidly dividing cells in the gastrointestinal tract and bone marrow, which dramatically **increases the risk of infection** due to:

- **Mucositis** – Damage to rapidly dividing epithelial cells of the digestive tract creates breaches in the mucosal barrier that allow **endogenous bacterial flora** (commensal organisms) to penetrate and enter the bloodstream. Gram-negative enteric bacilli, such as *Pseudomonas aeruginosa*, and gram-positive skin organisms, such as *Staphylococcus epidermidis* and *S aureus*, are most likely to invade.
- **Neutropenia** – Damage to rapidly dividing granulopoietic cells reduces circulating neutrophil count. Because neutrophils serve as front-line defense against bacterial and fungal pathogens, commensal pathogens that penetrate the mucosal/cutaneous barrier cannot be contained and subsequently spread to the bloodstream and deeper tissues. Neutropenic patients have weak inflammatory responses and **fever** is often the **only sign of infection** (neutropenic fever).

To reduce the risk of serious infection, patients who receive systemic chemotherapy are often empirically treated with prophylactic antibiotics (eg, ciprofloxacin) to prevent commensal organisms from invading and with granulocyte-stimulating agents (eg, filgrastim) to increase neutrophil count.

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(Choice A) Environmental pathogens such as *Histoplasma* (in bird droppings), Mycobacterium avium complex (in water), and *Cryptococcus* (in soil contaminated by bird droppings) often cause opportunistic infection in those with advanced AIDS due to impaired cell-mediated immunity. Although these pathogens can cause infections in those with neutropenia, most cases of neutropenic fever are due to endogenous commensal organisms.

(Choice B) Hospital-acquired, drug-resistant bacteria, such as methicillin-resistant *S aureus*, can cause neutropenic fever but do so much less often than endogenous commensal bacteria.

(Choice C) Pathogens spread from infected contacts (eg, influenza) are more likely to cause severe infection in those with impaired immunity. However, the greatest cause of neutropenic fever is endogenous bacterial flora.

(Choice E) The reactivation of latent bacterial (eg, tuberculosis) and viral (eg, cytomegalovirus) pathogens is common in those with impaired cellular immunity (eg, AIDS, immunosuppression). However, endogenous commensal bacteria are a more likely cause of fever in neutropenic patients.

Educational objective:
Chemotherapy-associated neutropenic fever is most often caused by endogenous commensal bacteria that

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(Choice B) Hospital-acquired, drug-resistant bacteria, such as methicillin-resistant *S aureus*, can cause neutropenic fever but do so much less often than endogenous commensal bacteria.

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(Choice E) The reactivation of latent bacterial (eg, tuberculosis) and viral (eg, cytomegalovirus) pathogens is common in those with impaired cellular immunity (eg, AIDS, immunosuppression). However, endogenous commensal bacteria are a more likely cause of fever in neutropenic patients.

Educational objective:
Chemotherapy-associated neutropenic fever is most often caused by endogenous commensal bacteria that have translocated across damaged mucosal sites.

References

- Microbial etiology of febrile neutropenia.

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A 24-year-old previously healthy man comes to the office due to a week of low-grade fever, malaise, sore throat, and persistent nonproductive cough. He does not use tobacco, alcohol, or illicit drugs. The patient takes no medications and has no drug allergies. He lives in Connecticut and has not traveled recently. Physical examination reveals mild pharyngeal erythema, no nasal congestion, and bilateral vesicular breath sounds with no crackles or wheezes. Chest x-ray shows patchy, interstitial infiltrates. Sputum Gram stain shows numerous leukocytes but no organisms. Which of the following agents is the best initial treatment for this patient?

A. Antagonist of folate metabolism
B. Inhibitor of bacterial cell wall synthesis
C. Inhibitor of bacterial protein synthesis
D. Inhibitor of ergosterol synthesis
E. Inhibitor of mycolic acid synthesis

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A. Antagonist of folate metabolism (3%)
B. Inhibitor of bacterial cell wall synthesis (5%)
✓ C. Inhibitor of bacterial protein synthesis (61%)
D. Inhibitor of ergosterol synthesis (15%)
E. Inhibitor of mycolic acid synthesis (13%)

61%
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10/07/2020

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This patient with low-grade fever, sore throat, persistent cough, and chest x-ray evidence of a bilateral patchy infiltrate likely has "walking pneumonia", a form of **atypical pneumonia** usually caused by ***Mycoplasma pneumoniae*** or *Chlamydia pneumoniae*.

Unlike most bacteria, *Mycoplasma* and *Chlamydia* do not have cell walls composed of peptidoglycan. *Mycoplasma* **completely lacks a cell wall**, while *Chlamydia* has a cell wall composed of an alternate protein. Therefore, these pathogens cannot be seen on Gram stain (which stains peptidoglycan) and cannot be treated with antibacterial agents that target peptidoglycan such as penicillins, cephalosporins, vancomycin, or carbapenems **(Choice B)**. Treatment requires a **bacterial protein synthesis inhibitor** such as a macrolide or tetracycline.

Legionella pneumophila is another common cause of atypical pneumonia. However, this pathogen usually is associated with gastrointestinal symptoms (eg, diarrhea), more severe clinical illness (eg, high fever), and lobar infiltrate on chest x-ray.

(Choice A) Trimethoprim and sulfamethoxazole are folate metabolism antagonists. They are the first-line therapy for *Pneumocystis* pneumonia, which often presents with subacute pulmonary symptoms and a bilateral patchy interstitial infiltrate. However, most patients have significant shortness of breath and nearly

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all are immunocompromised (eg, AIDS, chronic steroids).

(Choice D) Azole medications (eg, fluconazole) inhibit the synthesis of ergosterol, a primary component of the fungal cell membrane. Fungal pneumonias are often associated with lobar, nodular, or cavitary infiltrates. However, most occur in the setting of immunosuppression, and an accompanying sore throat would be unusual.

(Choice E) Mycolic acid is found in the cell wall of *Mycobacterium* and can be targeted by isoniazid, a mycolic acid synthesis inhibitor. Active pulmonary tuberculosis often presents with several weeks of cough, weight loss, malaise, and upper lobe cavitary infiltrates.

Educational objective:

Mycoplasma pneumoniae is a leading cause of atypical pneumonia. Because this pathogen lacks a cell wall, it does not show up on Gram stain and cannot be treated with beta-lactam antibiotics. Protein synthesis inhibitors (eg, macrolides, tetracycline) are the treatment of choice.

Microbiology	Infectious Diseases	Community acquired pneumonia
Subject	System	Topic

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A 26-year-old woman comes to the office due to fever, malaise, and joint pain. A week ago, the patient had pain in the small joints of her right hand, which improved spontaneously but was quickly followed by pain in the right ankle and left wrist. She has no prior medical problems and takes no medications. Temperature is 38 C (100.4 F), blood pressure is 124/82 mm Hg, and pulse is 90/min. The extremity joints are not erythematous or swollen, but tenderness is present along the tendons of the left wrist and right ankle. Several small, nontender pustules are seen on the extremities. There is no other rash. Blood culture in a selective growth medium consisting of chocolate agar and multiple antibiotics yields the causative pathogen. Which of the following strategies would most likely have prevented this patient's current condition?

A. Avoiding bites from ticks
B. Obtaining adequate vaccinations
C. Thoroughly cooking meat products
D. Using condoms consistently
E. Using mosquito repellents

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- A. Avoiding bites from ticks (7%)
- B. Obtaining adequate vaccinations (13%)
- C. Thoroughly cooking meat products (1%)
- D. Using condoms consistently (75%)
- E. Using mosquito repellents (1%)

Incorrect

75%

01 min, 32 secs

01/22/2021

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Disseminated gonococcal infection occurs when *Neisseria gonorrhoeae* spreads from the genitourinary tract to the bloodstream. It typically presents with the triad of polyarthralgia, tenosynovitis, and dermatitis (painless pustules on the extremities) or purulent arthritis. The diagnosis is confirmed when the organism is isolated on **Thayer-Martin media**, chocolate agar infused with antibiotics.

N gonorrhoeae is spread primarily via infected genital secretions during **sexual contact**. Therefore, most cases can be prevented by the **consistent use of condoms**, which act as a mucosal barrier between sexual partners. Patients with genitourinary *N gonorrhoeae* infections may have purulent cervicitis or urethritis, but many are asymptomatic. Asymptomatic infection increases the risk of spread to deeper tissues (eg, disseminated gonococcal infection, pelvic inflammatory disease) because of treatment delay.

(Choice A) Lyme disease is a tick-borne illness caused by the spirochete *Borrelia burgdorferi*. Early localized Lyme disease can be associated with arthralgias, myalgias, fever, and erythema migrans (a migrating, erythematous, bull's-eye rash). However, it is not associated with tendonitis/pustules, and spirochetes cannot be cultured on Thayer-Martin media.

(Choice B) *N gonorrhoeae* undergoes dramatic antigenic variation of its surface molecules, which prevents the formation of protective antibodies against future infection. Therefore, recurrent infection is

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(Choice B) *N gonorrhoeae* undergoes dramatic antigenic variation of its surface molecules, which prevents the formation of protective antibodies against future infection. Therefore, recurrent infection is common and vaccinations are ineffective.

(Choice C) The roundworm *Trichinella* can be transmitted via undercooked pork. It invades the skeletal muscle and causes severe muscle pain, swelling, and tenderness. Periorbital edema and eosinophilia are often important diagnostic clues. Diagnosis is made by serology; culture on Thayer-Martin media is not performed.

(Choice E) Dengue fever, also called breakbone fever, is a mosquito-borne viral infection associated with fever, severe myalgias, arthralgias, and macular rash. Hemorrhagic complications can occur. The diagnosis is usually made clinically; Thayer-Martin media would not yield an organism (as it is a viral pathogen).

Educational objective:
Neisseria gonorrhoeae is spread sexually by genitourinary secretions and can be prevented by the consistent use of condoms. Genitourinary infections are often asymptomatic, which increases the risk of spread through the bloodstream, leading to disseminated gonococcal infection. Patients with disseminated disease typically present with the triad of polyarthralgia, tenosynovitis, and dermatitis or purulent arthritis.

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A 42-year-old man comes to the physician because of dysuria and blood in his urine at the end of urination. He returned to the United States 2 weeks ago after several months touring Africa. While there, he went spelunking, bathed in the beaches and lakes, and ate the local street food. Physical examination is unremarkable. Ultrasonography reveals mild bilateral hydronephrosis and bladder wall thickening. Which of the following animals is the most likely source of this patient's infection?

A. Bat
B. Dog
C. Fish
D. Pig
E. Sheep
F. Snail

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A 42-year-old man comes to the physician because of dysuria and blood in his urine at the end of urination. He returned to the United States 2 weeks ago after several months touring Africa. While there, he went spelunking, bathed in the beaches and lakes, and ate the local street food. Physical examination is unremarkable. Ultrasonography reveals mild bilateral hydronephrosis and bladder wall thickening. Which of the following animals is the most likely source of this patient's infection?

- A. Bat (8%)
- B. Dog (2%)
- C. Fish (12%)
- D. Pig (3%)
- E. Sheep (2%)
- ✓ F. Snail (70%)

Correct

70% Answered correctly

28 secs Time Spent

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Schistosomiasis		
***Schistosoma* species**	**Location**	**Symptoms**
S haematobium	• North Africa • Sub-Saharan Africa • Middle East	**Urinary schistosomiasis** • Terminal hematuria, dysuria & frequent urination • Hydronephrosis, pyelonephritis & squamous cell carcinoma of the bladder
S mansoni	• Sub-Saharan Africa • Middle East • South America • Caribbean	**Intestinal schistosomiasis** • Diarrhea & abdominal pain • Intestinal ulceration → iron deficiency anemia
S japonicum	• Asia, particularly China • Philippines	**Hepatic schistosomiasis** • Hepatomegaly, splenomegaly • Periportal fibrosis & subsequent portal hypertension

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S japonicum	• Asia, particularly China • Philippines • Japan	**Hepatic schistosomiasis** • Hepatomegaly, splenomegaly • Periportal fibrosis & subsequent portal hypertension

This patient most likely has **schistosomiasis** caused by *Schistosoma haematobium*. Humans acquire schistosomiasis via contact with infected freshwater. Infection is not possible in the United States due to absence of the specific **freshwater snails** that incubate the infectious larvae.

Once released into the environment, the larvae can penetrate **intact human skin** and subsequently travel to the **liver** where they mature into adults over a period of several weeks. After maturation, the adult worms migrate to specific destinations: the mesenteric venules of the **intestine** (*S japonicum* and *S mansoni*) or the **urinary bladder** venous plexus (*S haematobium*). The adult worms remain in these blood vessels for life (5-30 years), adhering to the vessel wall with suckers and releasing eggs into circulation. Eggs released by *S japonicum* and *S mansoni* have a tendency to penetrate the bowel wall and be excreted in the feces. They also frequently traverse the portal venous system and lodge in the liver. *S haematobium* eggs tend to pierce the vesical and ureteral walls and be expelled in the urine. On exposure to freshwater, these eggs release larvae that can infect snails and perpetuate the life cycle.

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The clinical manifestations of schistosomiasis result from a **T_H2-mediated** granulomatous response directed against the eggs that is composed of infiltrating T_H2 cells, eosinophils, and M2 macrophages. This ultimately leads to the development of marked fibrosis and **ulceration and scarring of the bowel or bladder/ureters** (depending on the species). Eggs that settle into the presinusoidal radicals of the portal vein can cause **periportal "pipestem" fibrosis** (pathognomonic for hepatic schistosomiasis).

(Choice A) Bats are a major reservoir for the rabies virus.

(Choices B and E) The dog tapeworm *Echinococcus granulosus* is the most common cause of hydatid cysts in humans. Disease can occur following ingestion of foods contaminated with dog feces. Sheep are an intermediate host in this parasite's life cycle.

(Choice C) Infection with the human tapeworm *Diphyllobothrium latum* occurs due to the ingestion of larvae from raw freshwater fish. Disease classically results in vitamin B12 deficiency and megaloblastic anemia.

(Choice D) Human tapeworm infections caused by *Taenia solium* occur following consumption of larvae in infected undercooked pork. Cysticercosis is a disease caused by the larval stage of the organism following ingestion of eggs found in the excrement of *T solium* tapeworm carriers.

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(Choice C) Infection with the human tapeworm *Diphyllobothrium latum* occurs due to the ingestion of larvae from raw freshwater fish. Disease classically results in vitamin B12 deficiency and megaloblastic anemia.

(Choice D) Human tapeworm infections caused by *Taenia solium* occur following consumption of larvae in infected undercooked pork. Cysticercosis is a disease caused by the larval stage of the organism following ingestion of eggs found in the excrement of *T solium* tapeworm carriers.

Educational objective:

Humans acquire schistosomiasis via contact with freshwater sources that contain snails infected with *Schistosoma* larvae. *S japonicum* and *S mansoni* cause intestinal and hepatic schistosomiasis, and *S haematobium* causes urinary schistosomiasis.

References

- The Schistosoma granuloma: friend or foe?

Microbiology	Infectious Diseases	Schistosomiasis
Subject	System	Topic

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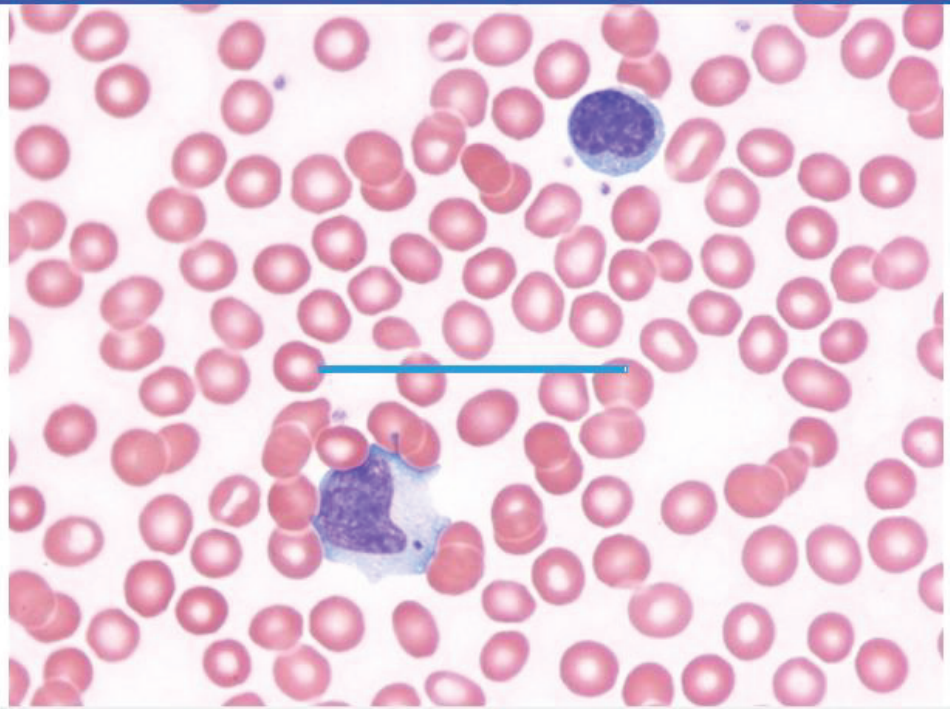
A 22-year-old woman comes to the office due to 2 weeks of profound fatigue, which has prevented her from attending college classes. The fatigue was preceded by fevers and sore throat, but these have now improved. The patient is an exchange student from Turkey and has no prior medical conditions. She does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Oropharyngeal examination shows no abnormalities. There are several enlarged lymph nodes posterior to the sternocleidomastoid muscle bilaterally. Cardiopulmonary examination is unremarkable. The spleen is palpable 1 cm below the left costal margin. No skin rashes or other lymphadenopathy is present. Peripheral blood evaluation shows increased numbers of abnormal white blood cells as shown in the exhibit. The observed cytoplasmic granules of these cells are most likely to contain which of the following substances?

A. Elastase
B. Immunoglobulins
C. Major basic protein
D. Perforin
E. Ribosomes

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Exhibit Display



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A. Elastase
B. Immunoglobulins
C. Major basic protein
D. Perforin
E. Ribosomes
F. Viral capsid

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A. Elastase (2%)
B. Immunoglobulins (16%)
C. Major basic protein (13%)
D. Perforin (37%)
E. Ribosomes (6%)
F. Viral capsid (22%)

Incorrect
Correct answer

37%

02 mins, 55 secs

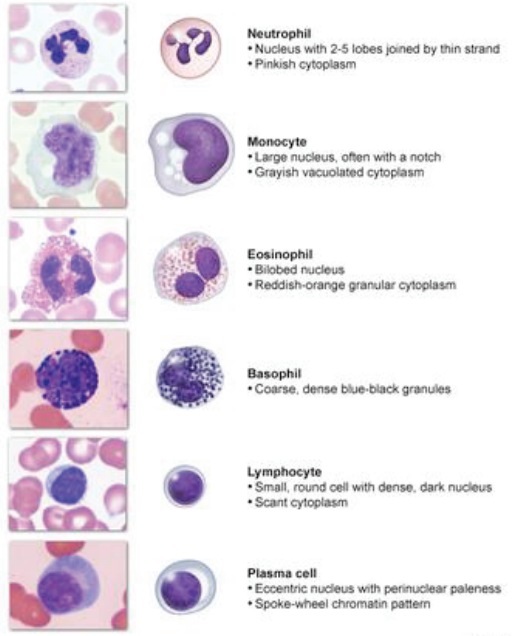
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Exhibit Display

Leukocytes in peripheral blood



Neutrophil
- Nucleus with 2-5 lobes joined by thin strand
- Pinkish cytoplasm

Monocyte
- Large nucleus, often with a notch
- Grayish vacuolated cytoplasm

Eosinophil
- Bilobed nucleus
- Reddish-orange granular cytoplasm

Basophil
- Coarse, dense blue-black granules

Lymphocyte
- Small, round cell with dense, dark nucleus
- Scant cytoplasm

Plasma cell
- Eccentric nucleus with perinuclear paleness
- Spoke-wheel chromatin pattern

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This patient's peripheral blood smear reveals a reactive (atypical) lymphocyte. In contrast to normal lymphocytes, which are small, round, and have minimal cytoplasm, reactive lymphocytes are large, **scalloped**, and have abundant cytoplasm.

Reactive lymphocytes are activated, pathogen-specific **cytotoxic T cells** and natural killer cells that form in response to certain **intracellular infections** (eg, HIV, cytomegalovirus, toxoplasmosis); they are particularly linked to **infectious mononucleosis**, a primary Epstein-Barr virus characterized by fever, pharyngitis, adenopathy, splenomegaly, and severe fatigue (as is likely in this patient).

Reactive lymphocytes are effector cells that contain **cytotoxic granules** composed of **perforin** (creates holes in the infected cell's membrane) and granzymes (enter the cytoplasm of infected cells and trigger cell death), which are released in response to foreign antigens on the surface (MHC class I receptors) of infected host cells.

(Choice A) Elastase breaks down collagen and is released by neutrophils and macrophages during acute inflammation. Neutrophils have multi-lobe nuclei and pinkish cytoplasm; macrophages have central round nuclei and abundant greyish, vacuolated cytoplasm. Neither typically has scalloped edges or abundant basophilic cytoplasm.

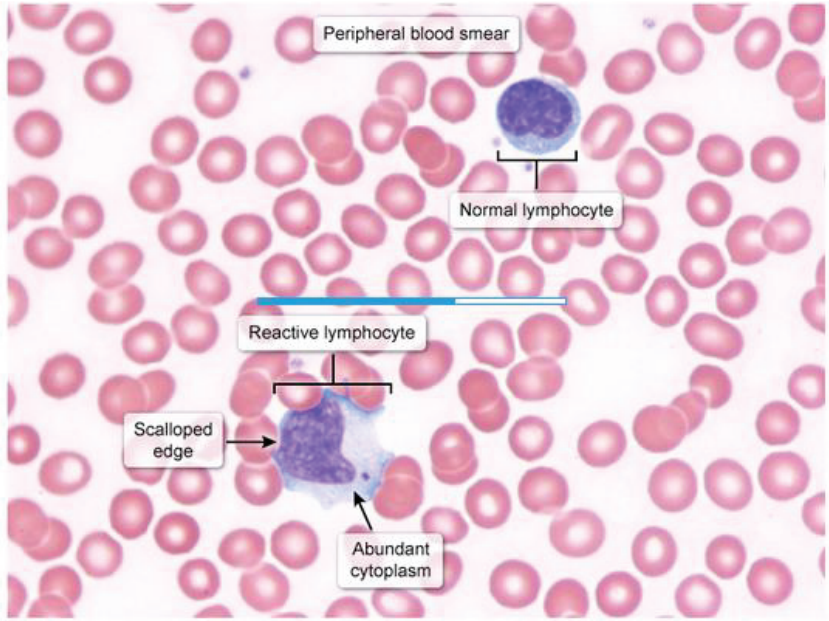
(Choice B) Immunoglobulins are secreted by plasma cells, which have an eccentric nucleus, perinuclear

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Exhibit Display

Reactive lymphocytes



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(Choice B) Immunoglobulins are secreted by plasma cells, which have an eccentric nucleus, perinuclear paleness (large Golgi apparatus), and spoke-wheel chromatin. Although immunoglobins cannot typically be visualized on light microscopy, immunoglobulin inclusions can sometimes be seen in plasma cell malignancies such as multiple myeloma (characterized by anemia, hypercalcemia, bone pain, and renal insufficiency).

(Choice C) Eosinophils generate and release major basic protein, which is the core constituent of eosinophilic granules; it acts as a cytotoxin and helminthotoxin and mediates epithelial damage, exfoliation, and bronchospasm in hypersensitivity diseases. Eosinophils have a bilobed nucleus and stain intensely pink.

(Choice E) Ribosomes generate proteins from messenger RNA; they can be visualized by electron microscopy but usually cannot be seen on light microscopy. However, ribosomal aggregates can sometimes be seen as basophilic stippling in patients with thalassemia or alcoholism.

(Choice F) Viral capsids are usually bound to viral genomes and shed in the cytoplasm prior to viral replication. This typically cannot be seen on light microscopy. Atypical lymphocytes are not infected by virus; they react to infected cells.

Educational objective:

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(Choice F) Viral capsids are usually bound to viral genomes and shed in the cytoplasm prior to viral replication. This typically cannot be seen on light microscopy. Atypical lymphocytes are not infected by virus; they react to infected cells.

Educational objective:
Reactive (atypical) lymphocytes are activated, pathogen-specific cytotoxic T cells or natural killer cells that form in response to certain intracellular infections. In contrast to normal lymphocytes, reactive lymphocytes are large, scalloped, and have abundant cytoplasm. Reactive lymphocytosis is a diagnostic feature of infectious mononucleosis.

Immunology	Infectious Diseases	Infectious mononucleosis
Subject	System	Topic

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A 3-year-old girl is brought to the emergency department with abrupt-onset vomiting followed by frequent, large-volume, watery diarrhea for the last day. She has no prior medical conditions but has not received recommended vaccinations. Temperature is 37.8 C (100 F). Physical examination shows mild dehydration. The abdomen is soft and mildly tender to palpation throughout. Bowel sounds are increased. Polymerase chain reaction testing of the stool sample yields a virus with a segmented, double-stranded RNA genome. Which of the following pathologic findings is most likely to be present in this patient?

A. Blunting of the villi in the duodenum and proximal jejunum

B. Extensive colonic mucosal injury with yellow-white adherent layer

C. Flask-shaped ulcerations in the cecum and ascending colon

D. Foamy macrophages in the small intestinal lamina propria

E. Inflammatory infiltration and necrosis of the Peyer patches

Submit

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A 3-year-old girl is brought to the emergency department with abrupt-onset vomiting followed by frequent, large-volume, watery diarrhea for the last day. She has no prior medical conditions but has not received recommended vaccinations. Temperature is 37.8 C (100 F). Physical examination shows mild dehydration. The abdomen is soft and mildly tender to palpation throughout. Bowel sounds are increased. Polymerase chain reaction testing of the stool sample yields a virus with a segmented, double-stranded RNA genome. Which of the following pathologic findings is most likely to be present in this patient?

A. Blunting of the villi in the duodenum and proximal jejunum (48%)
B. ~~Extensive colonic mucosal injury with yellow-white adherent layer~~ (9%)
C. ~~Flask-shaped ulcerations in the cecum and ascending colon~~ (3%)
D. ~~Foamy macrophages in the small intestinal lamina propria~~ (10%)
E. Inflammatory infiltration and necrosis of the Peyer patches (27%)

Correct

48%
Answered correctly

01 min, 38 secs
Time Spent

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Rotavirus is a segmented, nonenveloped, double-stranded RNA virus that is primarily transmitted via the fecal-oral route. It is a major cause of infectious diarrhea in children worldwide and typically presents in those **age <5** with acute, self-limited fever and **watery diarrhea** that may lead to **dehydration** and electrolyte abnormalities. Rotavirus vaccination is protective and has resulted in a dramatic reduction in disease incidence.

Rotavirus invades the villous epithelium of the **duodenum and proximal jejunum**. Infection causes diarrhea via multiple mechanisms including **villous blunting** (loss of absorptive capacity), proliferation of secretory crypt cells (secretory diarrhea), and reduced brush border enzymes (accumulation of unmetabolized disaccharides in the small intestine lumen). Rotavirus-induced diarrhea is noninflammatory; therefore, fecal leukocytes and erythrocytes are not typically seen. Repeat infections are often less severe than initial infection due to the generation of protective secretory IgA against rotaviral antigens.

(Choice B) *Clostridioides difficile* infection causes exotoxin-mediated damage to the large intestine mucosa, leading to the development of yellow-white pseudomembranes. Cases are most common after recent antibiotic therapy and usually present with watery diarrhea, fever, and abdominal pain. *C difficile* is a spore-forming, gram-positive bacterium.

(Choice C) *Entamoeba histolytica* is an anaerobic parasite that commonly causes dysentery and

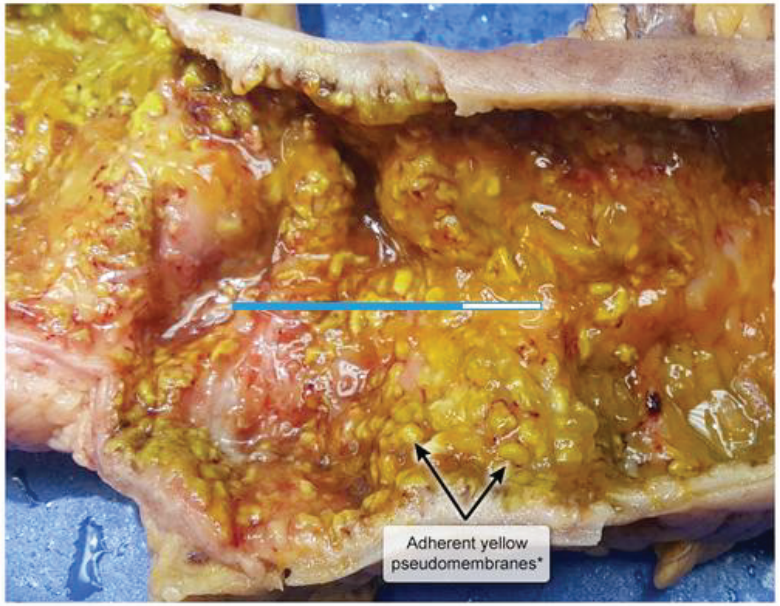
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Rotavirus is a segmented, nonenveloped, double-stranded RNA virus that is primarily transmitted via the

Exhibit Display

Pseudomembranous colitis



*Fibrin and inflammatory debris associated with *Clostridioides* (formerly *Clostridium*) *difficile*

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a spore-forming, gram-positive bacterium.

(Choice C) *Entamoeba histolytica* is an anaerobic parasite that commonly causes dysentery and extraintestinal disease (eg, liver abscess) in the developing world. Gastrointestinal infection usually results in bloody stools and fever; colonic visualization classically reveals flask-shaped ulcers (ie, with overhanging edges) in the cecum and ascending colon.

(Choice D) Whipple disease is caused by the gram-positive bacillus *Tropheryma whipplei*. Histopathology of the small intestine classically shows foamy macrophages in the lamina propria. Manifestations usually include arthralgias and chronic diarrhea with malabsorption and weight loss.

(Choice E) Typhoid strains of *Salmonella* pass through enterocytes and invade macrophages in the intestinal submucosa and Peyer patches. Inflammation and necrosis of Peyer patches can lead to life-threatening gastrointestinal bleeding and perforation.

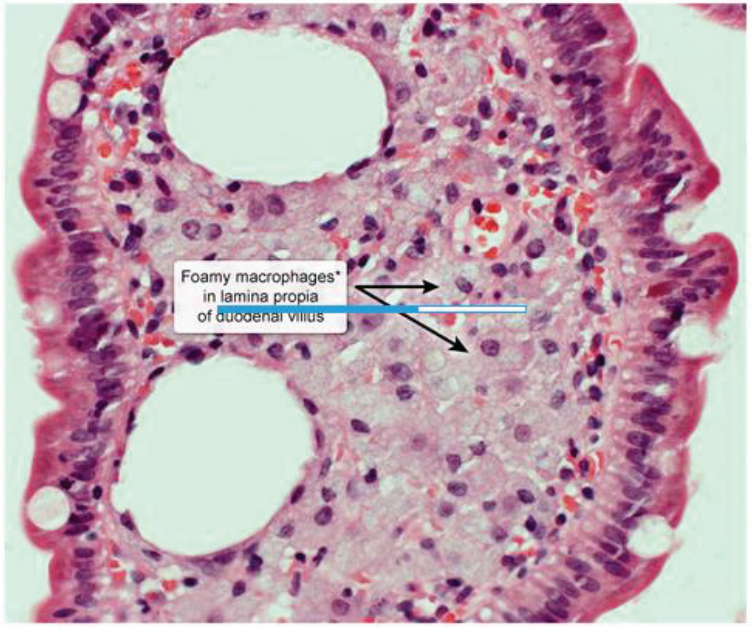
Educational objective:
Rotavirus is a common cause of self-limited childhood diarrhea in unvaccinated individuals. It infects villous enterocytes in the duodenum and proximal jejunum and results in villous blunting, proliferation of secretory crypt cells, and a loss of brush border enzymes; this results in watery diarrhea without fecal leukocytes.

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Exhibit Display

Whipple disease



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leukocytes.

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A 64-year-old man comes to the emergency department due to fever, anorexia, and nausea. He recently immigrated to the United States to live with his son. Several weeks ago, on routine testing, the patient was found to have a positive purified protein derivative test. He had no respiratory symptoms, and a chest x-ray was unremarkable. A month ago, he started isoniazid therapy with pyridoxine supplementation. Currently, temperature is 38.3 C (100.9 F). On physical examination, there is mild abdominal discomfort. Laboratory studies are pending. Which of the following is the most likely cause of this patient's current symptoms?

A. Factitious disorder
B. Gastric mucosal damage
C. Hepatocyte damage
D. Peripheral nerve damage
E. Serum sickness

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A. ~~Factitious disorder~~ (1%)
B. Gastric mucosal damage (8%)
C. Hepatocyte damage (73%)
D. Peripheral nerve damage (3%)
E. ~~Serum sickness~~ (12%)

Incorrect
Correct answer
C

73%
Answered correctly

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Time Spent

10/16/2020
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This patient with latent tuberculosis infection (positive tuberculin skin test, no symptoms, unremarkable chest x-ray) was started on **isoniazid** (INH) therapy and now has fever, anorexia, and nausea. INH is directly **hepatotoxic**. In 10%-20% of patients, it causes acute, **mild** hepatic dysfunction, characterized by transient increases in serum aminotransferases (AST/SGOT, ALT/SGPT). This adverse effect usually occurs during the first 4-6 months of treatment, and, in most cases, liver function tests return to baseline with continued INH therapy. In rare instances (<1%), frank **hepatitis** (similar to viral hepatitis with fever, anorexia, nausea, jaundice) can occur (as seen in this patient) and sometimes evolves into a **severe** form with progressive liver dysfunction and death.

(Choice A) Factitious disorder is the intentional falsification or inducement of symptoms with the goal of assuming the sick role. It is unlikely in this patient, who should be evaluated for INH hepatotoxicity.

(Choice B) Nonsteroidal anti-inflammatory drugs can cause gastric mucosal damage by inhibiting gastric prostaglandin production.

(Choice D) Peripheral neuropathy is also a potential side effect of INH therapy if simultaneous pyridoxine is not administered. However, peripheral neuropathy would not cause the above symptoms.

(Choice E) Serum sickness drug hypersensitivity generally causes fever, urticaria, arthralgias, proteinuria, and lymphadenopathy 5-10 days after exposure to the drug (antigen). This patient does not have

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(Choice E) Serum sickness drug hypersensitivity generally causes fever, urticaria, arthralgias, proteinuria, and lymphadenopathy 5-10 days after exposure to the drug (antigen). This patient does not have arthralgias or skin findings.

Educational objective:
Isoniazid can be directly hepatotoxic, causing acute, mild hepatic dysfunction in 10%-20% of patients and frank hepatitis (fever, anorexia, and nausea, sometimes progressing to hepatic failure) in a small percentage of patients.

Pharmacology	Infectious Diseases	Tuberculosis
Subject	System	Topic

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A 35-year-old woman, gravida 1, para 0, at 12 weeks gestation comes to the office for evaluation of genital warts. She first noticed the warts last week and is concerned that it has persisted. The patient has occasional mild pruritus but no pain. She is currently sexually active with her boyfriend and engages in oral and vaginal intercourse. Examination shows several verrucous, skin-colored lesions over the labia majora. The patient asks whether the lesion could affect her future child. The virus involved in this patient's condition also has an affinity to infect which of the following structures?

A. Alveoli
B. False vocal cords
C. Paranasal sinuses
D. Trachea
E. True vocal cords

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- A. Alveoli (4%)
- B. False vocal cords (25%)
- C. Paranasal sinuses (16%)
- D. Trachea (9%)
- ✓ E. True vocal cords (44%)

Correct

44% Answered correctly

26 secs Time Spent

02/16/2021 Last Updated

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Respiratory epithelium		
Type	**Location**	**Function**
Ciliated, pseudostratified, columnar	Nasal cavity, upper pharynx, false vocal cords, trachea, bronchi	• Mucus-secreting cells moisten air & trap debris/pathogens • Ciliary beating sweeps debris toward pharynx for swallowing
Squamous stratified	True vocal cords	Protects from abrasion & chemical attack
Cuboidal	Bronchioles	Conduct air to alveoli
Simple squamous	Alveoli	Gas exchange

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This patient's verrucous, skin-colored genital lesion is most consistent with condylomata acuminatum, also known as anogenital warts. Condylomata acuminatum is caused by **human papillomavirus (HPV)**, a small **double-stranded DNA virus** with >100 subtypes. HPV is the most common sexually transmitted disease and can be transmitted by vaginal, anal, and oral intercourse. Most infections are cleared by host

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This patient's verrucous, skin-colored genital lesion is most consistent with condylomata acuminatum, also known as anogenital warts. Condylomata acuminatum is caused by **human papillomavirus (HPV)**, a small **double-stranded DNA virus** with >100 subtypes. HPV is the most common sexually transmitted disease and can be transmitted by vaginal, anal, and oral intercourse. Most infections are cleared by host immunity, but **types 6** and **11** can result in warts.

HPV infects basal epithelial cells through small breaks in the skin or mucosal surfaces. It has a predilection for **stratified squamous epithelium**, which is found in the anal canal, vagina, and cervix. In the respiratory tract, the **true vocal cords** are the only area covered with stratified squamous epithelium. The vocal cords undergo near-constant friction and abrasion to produce speech. Stratified squamous epithelium is protective, as deeper cells can replace surface cells that are damaged.

Infants can acquire respiratory papillomatosis via passage through the birth canal of mothers infected with the virus. Warty growths on the true vocal cords can lead to a weak cry, hoarseness, and stridor.

(Choice A) The alveoli are comprised of simple squamous epithelium. This thin and flat epithelium facilitates rapid transmembrane exchange of oxygen and carbon dioxide.

(Choice B) The false vocal cords, also known as ventricular folds, are folds of mucous membrane lined in

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(Choice A) The alveoli are comprised of simple squamous epithelium. This thin and flat epithelium facilitates rapid transmembrane exchange of oxygen and carbon dioxide.

(Choice B) The false vocal cords, also known as ventricular folds, are folds of mucous membrane lined in respiratory epithelium, which is ciliated, pseudostratified, columnar, and mucus-secreting. The false vocal cords are adjacent to the true vocal cords and help to lubricate the true vocal cords with mucus and protect the airway from foreign bodies.

(Choices C and D) The paranasal sinuses and trachea also are lined in respiratory epithelium. This ciliated, pseudostratified, columnar, and mucus-secreting epithelium protects the respiratory tract from debris and pathogens. Goblet cells secrete mucus to trap particulate matter, and the cilia beat in a rhythmic fashion to propel this mucus/debris toward the oral cavity, where it can be swallowed or coughed up.

Educational objective:
Human papilloma virus (HPV) is a small DNA virus with a tropism for stratified squamous epithelium, which protectively lines anatomical areas that undergo frequent friction and abrasion, including the true vocal cords, cervix, and anus. Infants can acquire respiratory papillomatosis via passage through an HPV-infected birth canal.

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A 74-year-old man with end-stage renal disease who is receiving hemodialysis is found to have elevated liver transaminase levels. He has had no fever or jaundice. The patient does not drink alcohol and has received a complete vaccine series for hepatitis B. Vital signs are normal. BMI is 24 kg/m^2. Physical examination shows anicteric sclerae and no hepatosplenomegaly. Laboratory results are positive for hepatitis C virus RNA. Six months previously, he tested negative for hepatitis C. Without treatment, which of the following is the most likely outcome in this patient?

A. Acute liver failure
B. Decompensated liver cirrhosis
C. Hepatocellular carcinoma
D. Lifelong persistent infection
E. Spontaneous viral clearance

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A. Acute liver failure (4%)
B. Decompensated liver cirrhosis (12%)
C. Hepatocellular carcinoma (20%)
D. Lifelong persistent infection (51%)
E. Spontaneous viral clearance (10%)

Incorrect
Correct answer

51%
Answered correctly

57 secs
Time Spent

03/08/2021
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This patient has a new infection with **hepatitis C virus (HCV)**, presenting with elevated hepatic aminotransferases and confirmed on HCV RNA assay. The risk of HCV infection is elevated in patients on **hemodialysis** due to their frequent exposure to blood products, and these individuals are regularly screened for HCV.

Immediately after exposure to HCV, some patients develop jaundice, abdominal pain, and elevated aminotransferases (ie, acute hepatitis C), whereas others remain asymptomatic. Although some patients clear the virus spontaneously within 6 months of initial infection, the majority (50%-80%) remain persistently viremic and develop **chronic HCV** unless they receive treatment with antiviral medication **(Choice E)**. Viral persistence is even more likely in elderly or immunosuppressed individuals (eg, end-stage renal disease, HIV infection).

Most patients with chronic HCV exhibit nonspecific disease manifestations, including fatigue, abdominal pain, and elevations in aminotransferases. Approximately 20% of chronic HCV infections lead to cirrhosis, which takes decades (25-30 years) to develop. Of those with HCV-related cirrhosis, a small minority develop life-threatening hepatic decompensation (eg, esophageal variceal bleeding, ascites) or hepatocellular carcinoma **(Choices B and C)**. Given this patient's age and comorbidities, he is unlikely to survive long enough to develop cirrhosis or carcinoma.

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which takes decades (25-30 years) to develop. Of those with HCV-related cirrhosis, a small minority develop life-threatening hepatic decompensation (eg, esophageal variceal bleeding, ascites) or hepatocellular carcinoma **(Choices B and C)**. Given this patient's age and comorbidities, he is unlikely to survive long enough to develop cirrhosis or carcinoma.

(Choice A) Acute HCV can cause acute (eg, fulminant) liver failure, a life-threatening condition characterized by encephalopathy and impaired hepatic synthetic function (eg, prolonged prothrombin time). However, this is a rare manifestation and is much less common than chronic HCV.

Educational objective:
The most common outcome of hepatitis C infection without antiviral treatment is lifelong persistent infection (ie, chronic hepatitis C). Of those with chronic hepatitis C, approximately 20% develop cirrhosis, and only a minority experiences complications (eg, ascites, variceal bleeding, hepatocellular carcinoma).

References

- Natural history of hepatitis C.
- Hepatitis C cirrhosis: new perspectives for diagnosis and treatment.

Microbiology Infectious Diseases Hepatitis c

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A microbiologist performs a genetic experiment in which cultures of *Escherichia coli* are treated with a chemical that induces a high frequency of mutations. Individual bacterial colonies are isolated to identify a mutant strain that lacks a specific enzyme involved in DNA replication. This specific enzyme is responsible for removing short fragments of RNA that are base paired to the DNA template. Which of the following enzymes is most likely deficient in this strain of *E coli*?

A. DNA polymerase I
B. DNA polymerase III
C. Gyrase
D. Helicase
E. Ligase
F. Primase

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- A. DNA polymerase I (55%)
- B. DNA polymerase III (17%)
- C. Gyrase (3%)
- D. Helicase (1%)
- E. Ligase (8%)
- F. Primase (13%)

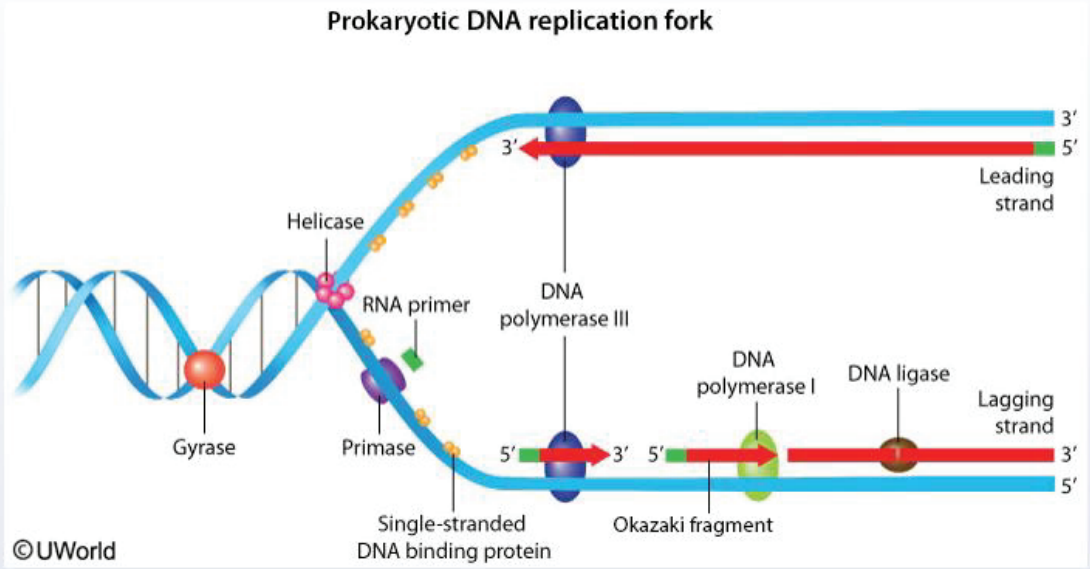
Correct

55%
Answered correctly

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Time Spent

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Bacterial DNA replication is coordinated by the actions of multiple enzymes and proteins. Before DNA synthesis begins, helicase binds double-stranded DNA at the origin of replication with the assistance of DnaA protein and acts at the replication fork to unwind and separate the DNA **(Choice D)**. Single-stranded DNA-binding protein then attaches to the separated strands to prevent their reannealing. Unwinding and separation of DNA produces positive supercoils that can lead to DNA fracture if not relieved.

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Proteins & their function in prokaryotic DNA replication	
Helicase	Unwinding of double helix
Topoisomerase II (DNA gyrase)	Removal of supercoils
Single-stranded DNA-binding protein	Stabilization of unwound template strands
Primase (RNA polymerase)	Synthesis of RNA primer
DNA polymerase III	5' to 3' DNA synthesis & 3' to 5' exonuclease ("proofreading") activity
DNA polymerase I	Same as DNA polymerase III Also removes RNA primer (5' to 3' exonuclease activity) & replaces it with DNA
DNA ligase	Joining of Okazaki fragments (lagging strand)

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separation of DNA produces positive supercoils that can lead to DNA fracture if not relieved. Topoisomerase II (DNA gyrase) relieves the tension created during unwinding by introducing negative supercoils into the DNA **(Choice C)**.

Before DNA polymerase III can begin elongating a new DNA strand, it requires an RNA primer made up of short RNA sequences base-paired to the parent DNA. This primer is synthesized by the enzyme primase (DNA-dependent RNA polymerase) **(Choice F)**. DNA synthesis then proceeds in the 5' to 3' direction with the leading strand being formed continuously toward the replication fork and the lagging strand being formed discontinuously away from the replication fork. Replication of the lagging strand results in the formation of numerous short DNA segments called Okazaki fragments. These fragments are ultimately bound together by the enzyme ligase after their RNA primers have been removed and replaced with DNA **(Choice E)**.

The **removal of RNA primers** and their replacement with DNA is accomplished by **DNA polymerase I**, the only bacterial DNA polymerase with **5' to 3' exonuclease activity**. DNA polymerase III has 5' to 3' polymerase and 3' to 5' exonuclease ("proofreading") activity; however, it cannot remove RNA primers as it lacks 5' to 3' exonuclease activity **(Choice B)**.

Educational objective:

During bacterial DNA replication, DNA polymerase I functions to remove RNA primers (via 5' to 3'

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short RNA sequences base-paired to the parent DNA. This primer is synthesized by the enzyme primase (DNA-dependent RNA polymerase) **(Choice F)**. DNA synthesis then proceeds in the 5' to 3' direction with the leading strand being formed continuously toward the replication fork and the lagging strand being formed discontinuously away from the replication fork. Replication of the lagging strand results in the formation of numerous short DNA segments called Okazaki fragments. These fragments are ultimately bound together by the enzyme ligase after their RNA primers have been removed and replaced with DNA **(Choice E)**.

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Educational objective:
During bacterial DNA replication, DNA polymerase I functions to remove RNA primers (via 5' to 3' exonuclease activity) and replace them with DNA (via 5' to 3' polymerase activity). DNA polymerase I is the only bacterial DNA polymerase that possesses 5' to 3' exonuclease activity.

References

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A 42-year-old man comes to the emergency department due to fever, abdominal pain, and explosive diarrhea. He has a history of HIV but has not been taking any medications. BMI is 18.2 kg/m^2. Abdominal examination is notable for right-sided tenderness to palpation. Laboratory results show a CD4 cell count of 38/mm^3, leukopenia, and thrombocytopenia. A CT scan of the abdomen reveals colitis. Colonoscopy reveals areas of erosions and ulcerations; pathology demonstrates cells with viral intranuclear and intracytoplasmic inclusions. Antiviral therapy is initiated to treat the colitis with an intravenous agent that does not require intracellular activation and is known to bind in vitro with viral-encoded enzymes such as DNA polymerase, RNA polymerase, and reverse transcriptase. Which of the following agents did this patient most likely receive?

A. Acyclovir
B. Foscarnet
C. Ganciclovir
D. Lamivudine
E. Oseltamivir

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38/mm³, leukopenia, and thrombocytopenia. A CT scan of the abdomen reveals colitis. Colonoscopy reveals areas of erosions and ulcerations; pathology demonstrates cells with viral intranuclear and intracytoplasmic inclusions. Antiviral therapy is initiated to treat the colitis with an intravenous agent that does not require intracellular activation and is known to bind in vitro with viral-encoded enzymes such as DNA polymerase, RNA polymerase, and reverse transcriptase. Which of the following agents did this patient most likely receive?

- A. Acyclovir
- B. Foscarnet
- C. Ganciclovir
- D. Lamivudine
- E. Oseltamivir
- F. Saquinavir
- G. Sofosbuvir

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reveals areas of erosions and ulcerations; pathology demonstrates cells with viral intranuclear and intracytoplasmic inclusions. Antiviral therapy is initiated to treat the colitis with an intravenous agent that does not require intracellular activation and is known to bind in vitro with viral-encoded enzymes such as DNA polymerase, RNA polymerase, and reverse transcriptase. Which of the following agents did this patient most likely receive?

- A. ~~Acyclovir~~ (3%)
- ✓ B. Foscarnet (56%)
- C. Ganciclovir (16%)
- D. ~~Lamivudine~~ (13%)
- E. ~~Oseltamivir~~ (3%)
- F. ~~Saquinavir~~ (3%)
- G. ~~Sofosbuvir~~ (3%)

Correct

56%
Answered correctly

01 min, 31 secs
Time Spent

10/04/2020
Last Updated

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This patient with HIV likely has cytomegalovirus (CMV) colitis (intranuclear and intracytoplasmic inclusions), which, in some patients (eg, with ganciclovir resistance or refractory thrombocytopenia), is treated with foscarnet. **Foscarnet** is a pyrophosphate analog that does **not** require intracellular activation. It directly inhibits both DNA polymerase in herpesvirus and reverse transcriptase in HIV. Foscarnet must be administered intravenously. In addition to treating ganciclovir-resistant CMV infections, foscarnet is useful in patients who have acyclovir-resistant herpesvirus infections. **Ganciclovir**, a guanine nucleoside analogue structurally similar to acyclovir, is often used for CMV infections. However, it requires intracellular conversion by a virally encoded kinase and then by cellular kinases **(Choice C)**.

(Choice A) Acyclovir is a nucleoside analog that must be converted intracellularly to its monophosphate form by a virally encoded thymidine kinase. Cellular kinases convert the monophosphate form into a triphosphate form, which inhibits herpesvirus DNA polymerase-mediated replication.

(Choice D) Lamivudine is a cytosine analog classified as a nucleoside reverse transcriptase inhibitor. It must be phosphorylated to its active form, lamivudine triphosphate, by intracellular kinases. Lamivudine inhibits HIV reverse transcription through viral DNA chain termination.

(Choices E and F) Oseltamivir and saquinavir do not require intracellular activation but are not used for CMV infection. Oseltamivir is a sialic acid analogue inhibitor of influenza A and B virus neuraminidase.

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(Choice D) Lamivudine is a cytosine analog classified as a nucleoside reverse transcriptase inhibitor. It must be phosphorylated to its active form, lamivudine triphosphate, by intracellular kinases. Lamivudine inhibits HIV reverse transcription through viral DNA chain termination.

(Choices E and F) Oseltamivir and saquinavir do not require intracellular activation but are not used for CMV infection. Oseltamivir is a sialic acid analogue inhibitor of influenza A and B virus neuraminidase. Saquinavir is an HIV protease inhibitor that prevents the cleavage of polyprotein precursors necessary for the generation of functional viral proteins.

(Choice G) Sofosbuvir inhibits nonstructural protein 5B (NS5B), an RNA-dependent RNA polymerase needed for hepatitis C virus replication. It requires intracellular activation.

Educational objective:
Of all the antiviral agents that bind and inhibit DNA polymerase in herpesvirus and reverse transcriptase in HIV, the pyrophosphate analog foscarnet is one of few that do not require intracellular activation by viral or cellular kinases.

Pharmacology Infectious Diseases Cytomegalovirus

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A 24-year-old man develops mild, nonexudative pharyngitis shortly after travel to Eastern Europe. Throat swab culture in tellurite-containing, selective media yields black, iridescent colonies. Microscopy shows club-shaped, gram-positive bacilli in a palisade arrangement, which are identified as nonpathogenic *Corynebacterium diphtheriae*. These bacteria can acquire virulence to become pathogenic through which of the following mechanisms?

A. Bacterial conjugation permitting pili expression
B. Chromosomal mutation permitting endotoxin production
C. Environmental influences permitting toxin synthesis
D. Phage conversion permitting exotoxin production
E. Transformation permitting capsule formation

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A. ~~Bacterial conjugation permitting pili expression~~ (9%)
B. Chromosomal mutation permitting endotoxin production (6%)
C. Environmental influences permitting toxin synthesis (10%)
D. Phage conversion permitting exotoxin production (70%)
E. ~~Transformation permitting capsule formation~~ (3%)

Correct

70%
Answered correctly

01 min, 34 secs
Time Spent

02/03/2021
Last Updated

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Corynebacterium diphtheriae is a non-spore–forming, gram-positive bacillus that is transmitted primarily via aerosolized droplets. Nontoxigenic strains are minimally infectious; toxigenic strains are virulent and cause the clinical syndrome of **diphtheria**. Conversion from nontoxigenic to toxigenic *C diphtheriae* occurs due to infection with a **lysogenic bacteriophage** called Corynephage beta. This phage inserts the *tox* gene into the *C diphtheriae* genome, which results in the bacterial expression of the **diphtheria AB toxin**. Diphtheria toxin irreversibly halts protein synthesis due to ADP-ribosylation of elongation factor-2 and causes severe local (eg, pseudomembranous pharyngitis) and systemic (eg, myocarditis, neuritis) effects.

(Choice A) Conjugation is the direct transfer of plasmids from one bacterium to another through a pilus. Genes for antibiotic resistance are often transmitted in this manner.

(Choice B) Chromosomal mutations can theoretically lead to endotoxin production, but mutations more commonly lead to bacterial antibiotic resistance.

(Choice C) The gram-positive, spore-forming rods *Bacillus* and *Clostridium* generate toxins under environmental influences. The *B anthracis* spore, the causative agent in anthrax, survives in soil for extended periods in a state of dormancy. Only upon warming to 37° C in the presence of appropriate concentrations of CO_2 and protein do the spores germinate and begin to synthesize toxin. The case is

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environmental influences. The *B anthracis* spore, the causative agent in anthrax, survives in soil for extended periods in a state of dormancy. Only upon warming to 37° C in the presence of appropriate concentrations of CO_2 and protein do the spores germinate and begin to synthesize toxin. The case is similar for *C tetani* spores, which germinate and produce toxin only in anaerobic environments, such as necrotic wounds.

(Choice E) Transformation involves the direct uptake of genetic material from the environment with subsequent incorporation into the bacterial genome. *Streptococcus pneumoniae* acquires the ability to produce capsules via transformation. The capsule is the major virulence factor for *S pneumoniae*; strains without the capsule are not pathogenic.

Educational objective:
Lysogenic bacteriophages are responsible for converting nonpathogenic *Corynebacterium* into toxigenic *Corynebacterium*. Toxigenic strains elaborate the diphtheria exotoxin, which causes pseudomembranous pharyngitis and potentially life-threatening systemic effects (eg, myocarditis, neuritis).

Microbiology	Infectious Diseases	Diphtheria
Subject	System	Topic

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A 27-year-old man comes to the emergency department due to 2 weeks of low-grade fever, malaise, and loss of appetite. The patient has no prior medical conditions and takes no medications. He does not smoke cigarettes or drink alcohol but regularly injects illicit drugs. The patient is sexually active and uses condoms inconsistently. Physical examination reveals scleral icterus. A smooth and mildly tender liver edge is palpable 4 cm below the right costal margin. Laboratory results are as follows:

Liver function studies	
Total bilirubin	4.3 mg/dL
Alkaline phosphatase	220 U/L
Aspartate aminotransferase (SGOT)	1,600 U/L
Alanine aminotransferase (SGPT)	2,100 U/L
Hepatitis panel	
Hepatitis A virus antibody, IgM	negative
Hepatitis B surface antibody (HBsAb)	negative

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Hepatitis panel

Hepatitis A virus antibody, IgM	negative
Hepatitis B surface antibody (HBsAb)	negative
Hepatitis B core antibody (HBcAb), IgM	positive
Hepatitis B surface antigen (HBsAg)	positive
Hepatitis C virus antibody	negative

Which of the following is an essential step in the replication cycle of the virus infecting this patient?

A. Cleavage of precursor polyprotein by viral protease
B. Expression of regulatory latency-associated transcript
C. Integration of viral DNA into the host genome
D. Release of new viral particles by host cell lysis
E. Reverse transcription of template RNA to viral DNA

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Hepatitis A virus antibody, IgM	negative
Hepatitis B surface antibody (HBsAb)	negative
Hepatitis B core antibody (HBcAb), IgM	positive
Hepatitis B surface antigen (HBsAg)	positive
Hepatitis C virus antibody	negative

Which of the following is an essential step in the replication cycle of the virus infecting this patient?

A. ~~Cleavage of precursor polyprotein by viral protease~~ (4%)

B. ~~Expression of regulatory latency-associated transcript~~ (4%)

C. Integration of viral DNA into the host genome (31%)

D. ~~Release of new viral particles by host cell lysis~~ (8%)

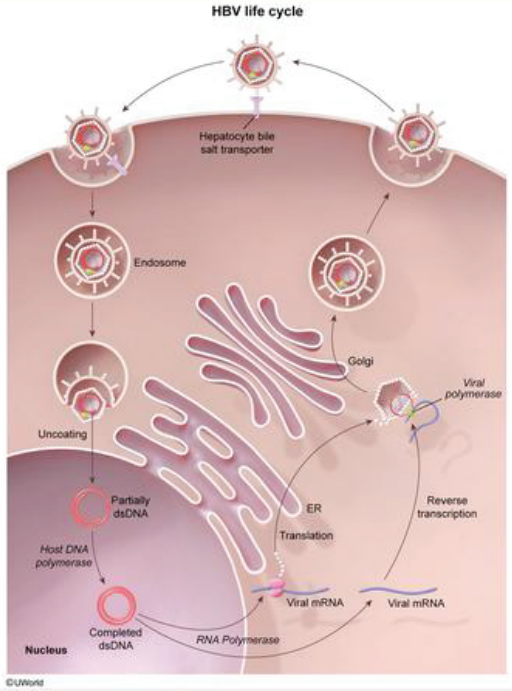
E. Reverse transcription of template RNA to viral DNA (50%)

50% 02 mins, 29 secs 10/26/2020

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Acute hepatitis B virus (HBV) infection is associated with the shedding of viral antigens (HBsAg, HBeAg) and HBV DNA into the bloodstream and the development of IgM antibodies against HBc. Patients are often asymptomatic, but a minority develops constitutional symptoms (eg, fatigue, loss of appetite), hepatomegaly, icterus, and significant elevations in aminotransferase levels. Transmission in low-prevalence countries (eg, United States) is usually due to injection drug use or unprotected sex.

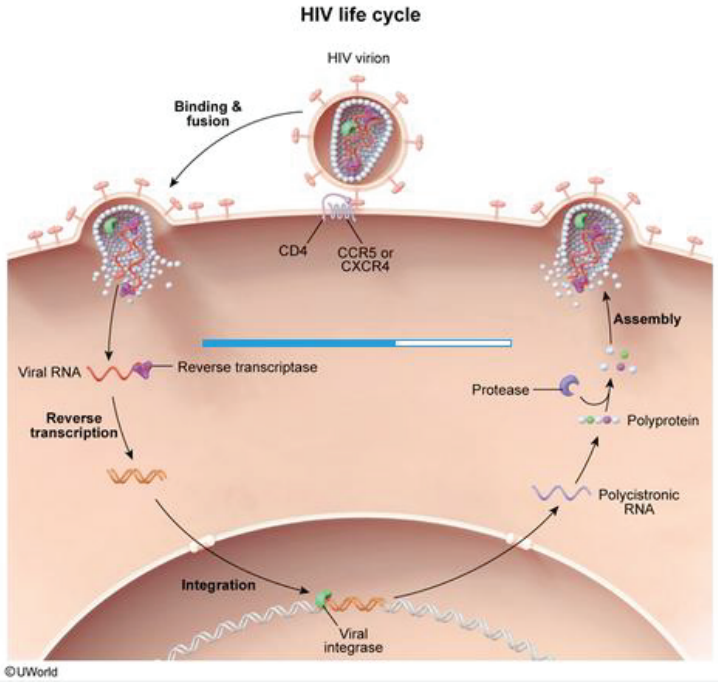
HBV is an encapsulated virus with a partially double-stranded DNA genome. It binds to and enters hepatocytes using a host cell bile salt transporter and then sheds its coat in the host cytoplasm. The partially double-stranded genome is "repaired" and transcribed by host cell machinery, yielding a **+ sense single-stranded mRNA template**. This serves as a **pre-genome** for future progeny; it is converted by **viral reverse transcriptase** into the partially double-stranded DNA genome of budding viral particles (which are subsequently released from the cell). The mRNA template is also translated by host ribosomes into the proteins that compose the virus.

(Choice A) Both hepatitis C virus and HIV encode for a viral protease that cleaves viral polyprotein into individual proteins. Protease inhibitors target this step in viral replication and are used for treatment. HBV does not generate a polyprotein; therefore, it does not encode for a viral protease.

(Choice B) Herpes simplex virus type 1 establishes a life-long latent infection within sensory neurons

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[Choice B] Herpes simplex virus type 1 establishes a life-long latent infection within sensory neurons

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(Choice B) Herpes simplex virus type 1 establishes a life-long latent infection within sensory neurons where it expresses latency-associated transcript, a non-protein coding RNA molecule that suppresses viral lytic genes and inhibits host cell apoptosis.

(Choice C) Although HBV can insert its genome into host chromosomes (which contributes to hepatocarcinogenesis), this step is not required for viral replication. In contrast, HIV must integrate into the host genome in order to replicate. Integrase inhibitors (eg, dolutegravir) target this step in HIV replication.

(Choice D) HBV is released via exocytosis from host cells and is not considered a lytic virus. Hepatocyte damage occurs primarily when cytotoxic T cells recognize HBV antigens on infected cells. Patients who clear the virus have a robust, polyclonal, cytotoxic T-cell response. Those that develop latent infection often have a much weaker and narrower cytotoxic T-cell response.

Educational objective:
Hepatitis B virus has a partially double-stranded DNA genome and contains a viral DNA polymerase with reverse transcriptase activity. Reverse transcriptase serves a crucial step in viral replication; it converts transcribed positive sense single-stranded RNA into the partially double-stranded DNA genome of viral progeny.

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A 22-year-old woman comes to the emergency department with fevers and arthralgias. She recently had unprotected sexual intercourse with a new male partner. Her temperature is 38.4 C (101.1 F), blood pressure is 118/76 mm Hg, pulse is 102/min, and respirations are 16/min. Examination shows several pustules on the dorsal aspects of her forearms. Her right wrist and ankle are tender on palpation. Gram-negative bacteria isolated from this patient's blood produce an enzyme that splits the IgA molecule at the hinge region. Which of the following is likely to be the most important role of this bacterial enzyme in the course of the infection?

A. It facilitates mucosal adherence of bacteria
B. It impairs complement-mediated cell lysis
C. It impairs opsonization and phagocytosis
D. It impairs secondary immune response generation
E. It promotes intracellular survival

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- A. It facilitates mucosal adherence of bacteria (59%)
- B. It impairs complement-mediated cell lysis (8%)
- C. It impairs opsonization and phagocytosis (23%)
- D. It impairs secondary immune response generation (5%)
- E. It promotes intracellular survival (3%)

50%
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02/13/2021

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This patient likely has disseminated gonorrheal infection (triad of arthritis, dermatitis, and tenosynovitis in a sexually active woman) due to *Neisseria gonorrhoeae*. In mucosal regions as well as in secretions, IgA exists in its secretory form, composed of an IgA dimer (joined by a peptide J chain) and a peptide secretory component. IgA antibodies usually bind to pili and other membrane proteins involved in bacterial adherence to mucosa, thus inhibiting mucosal colonization by the microorganism.

Certain bacteria (eg, *N gonorrhoeae, N meningitidis, Streptococcus pneumoniae, Haemophilus influenzae*) produce **IgA proteases** that cleave IgA at its hinge region (yielding Fab and compromised Fc fragments), thus decreasing its effectiveness. This facilitates **bacterial adherence to mucosa** (possibly due to easier bacterial access to mucosal surface or immune disguise by binding to released Fab fragments, among others).

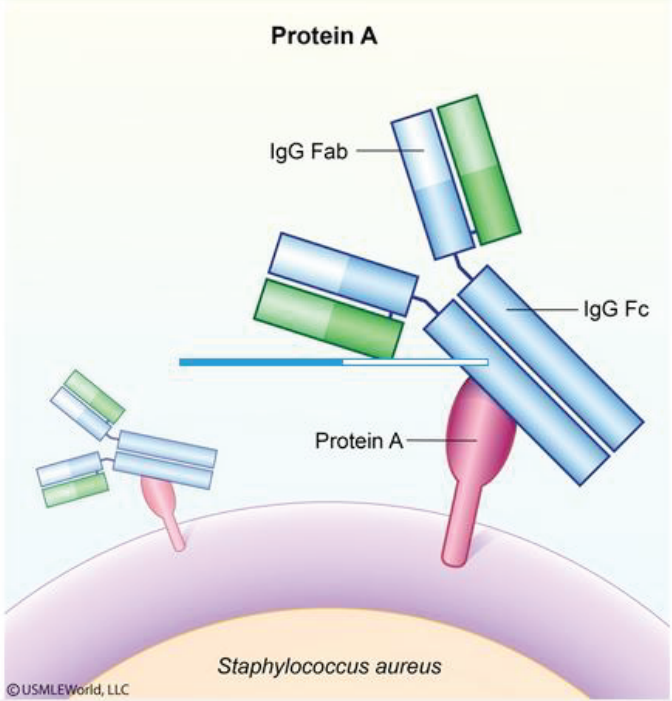
(Choice B) IgA is a weak activator of the classic complement pathway. Impairment of complement-mediated cell lysis can be accomplished by staphylococcal protein A, which binds the Fc portion of IgG, preventing complement fixation.

(Choice C) Although IgA Fc-mediated functions such as opsonization are compromised by IgA protease, secretory IgA is a poor opsonin. Impairment of opsonization and phagocytosis is most frequently

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(Choice C) Although IgA Fc-mediated functions such as opsonization are compromised by IgA protease, secretory IgA is a poor opsonin. Impairment of opsonization and phagocytosis is most frequently accomplished by encapsulated bacteria such as *S pneumoniae, N meningitidis*, and *H influenzae*.

(Choice D) IgA does not play a role in the induction of memory lymphocytes necessary for mounting a secondary immune response (which requires the formation of memory B and T lymphocytes after initial antigen exposure).

(Choice E) Promotion of intracellular survival is accomplished by inhibition of phagosome-lysosome fusion or resistance to lysosomal enzymes. These properties are expressed by *Mycobacterium tuberculosis, M leprae, Legionella*, and *Ehrlichia*.

Educational objective:

IgA protease is produced by *Neisseria meningitidis, N gonorrhoeae, Streptococcus pneumoniae*, and *Haemophilus influenzae*. This enzyme cleaves secretory IgA at its hinge region, rendering it ineffective. Secretory IgA exists on mucosal surfaces and in secretions and acts to bind and inhibit the action of pili as well as other cell surface antigens that normally mediate mucosal adherence and subsequent penetration.

References

- Working mechanism of immunoglobulin A1 (IgA1) protease: Cleavage of IgA1 antibody to Neisseria

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An 84-year-old woman is sent to the hospital from a nursing home due to 3 days of fever, abdominal pain, and progressive lethargy. The patient has a history of recurrent hospitalizations with multiple antibiotic courses for urinary tract infection, infected decubitus ulcer, and pneumonia. Her temperature is 38.2 C (101 F), blood pressure is 100/60 mm Hg, and pulse is 110/min. She has mild suprapubic and right costovertebral angle tenderness. Urine and blood cultures are obtained, and the patient is started on intravenous fluids and empiric ceftriaxone. Her urine culture shows extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli*. Which of the following features is most likely to be found in this organism?

A. DNA gyrase with altered A subunit
B. Outer membrane with novel porin structure
C. Penicillin-binding protein with reduced antibiotic affinity
D. Peptidoglycan cell wall with amino acid modification
E. Plasmid with drug resistance gene
F. Ribosome with methylated 16S rRNA

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courses for urinary tract infection, infected decubitus ulcer, and pneumonia. Her temperature is 38.2 C (101 F), blood pressure is 100/60 mm Hg, and pulse is 110/min. She has mild suprapubic and right costovertebral angle tenderness. Urine and blood cultures are obtained, and the patient is started on intravenous fluids and empiric ceftriaxone. Her urine culture shows extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli*. Which of the following features is most likely to be found in this organism?

A. ~~DNA gyrase with altered A subunit~~ (1%)

B. ~~Outer membrane with novel porin structure~~ (4%)

C. Penicillin-binding protein with reduced antibiotic affinity (30%)

D. ~~Peptidoglycan cell wall with amino acid modification~~ (9%)

✓ E. Plasmid with drug resistance gene (52%)

F. ~~Ribosome with methylated 16S rRNA~~ (1%)

Correct

52%

01 min, 25 secs

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Common antibiotic resistance mechanisms	
Penicillins	• Beta-lactamase, ESBL • Mutated PBP • Mutated porin protein
Vancomycin	• Mutated peptidoglycan cell wall • Impaired influx/increased efflux
Quinolones	• Mutated DNA gyrase • Impaired influx/increased efflux
Aminoglycosides	• Aminoglycoside-modifying enzymes • Mutated ribosomal subunit protein • Mutated porin protein
Tetracyclines	• Impaired influx/increased efflux • Inactivated enzyme
Rifamycins	• Mutated RNA polymerase

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Rifamycins	• Mutated RNA polymerase

ESBL = extended-spectrum beta-lactamase; **PBP** = penicillin-binding protein.

This patient has a urinary tract infection caused by an **extended-spectrum beta-lactamase** (ESBL)-producing *Escherichia coli*. ESBL enzymes can inactivate extended-spectrum penicillins and cephalosporins (including third- and fourth-generation cephalosporins) and monobactams (aztreonam). Genes encoding these enzymes are often located on **plasmids** and therefore can be transferred between organisms and between different species through conjugation. Some have been incorporated into bacterial chromosomes. **Carbapenems** (eg, imipenem) are the treatment of choice for ESBL-producing organisms (although unfortunately, organisms with carbapenem resistance have emerged).

(Choice A) Mutations in DNA gyrase can lead to fluoroquinolone resistance and generally do not impact beta-lactam antibiotic activity.

(Choice B) Porin mutations can confer penicillin and aminoglycoside resistance and are particularly important in gram-negative organisms such as *Pseudomonas*.

(Choice C) Penicillin-binding protein alterations are the mechanism that leads to methicillin resistance in *Staphylococcus aureus*.

(Choice D) Vancomycin inhibits glycopeptide polymerization through binding to D-alanyl-D-alanine in the

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beta-lactam antibiotic activity.

(Choice B) Porin mutations can confer penicillin and aminoglycoside resistance and are particularly important in gram-negative organisms such as *Pseudomonas*.

(Choice C) Penicillin-binding protein alterations are the mechanism that leads to methicillin resistance in *Staphylococcus aureus*.

(Choice D) Vancomycin inhibits glycopeptide polymerization through binding to D-alanyl-D-alanine in the cell wall precursor; peptidoglycan changes (eg, D-alanine-D-lactate) can develop as a resistance mechanism.

(Choice F) Ribosome mutations can confer resistance to ribosome-targeting antibiotics such as aminoglycosides and macrolides.

Educational objective:
Extended-spectrum beta-lactamases can be produced by gram-negative bacteria, rendering cephalosporins and other beta-lactam antibiotics inactive. These genes can be transmitted between organisms through plasmid conjugation.

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An 86-year-old woman is hospitalized for a urinary tract infection due to *Escherichia coli* and is being treated with ceftriaxone. She has a history of advanced dementia, coronary artery disease, and congestive heart failure. On the fifth day of hospitalization, she seems agitated. The nurse also reports that the patient had 3 episodes of diarrhea the previous night. Her temperature is 38.3 C (101 F). In addition to appropriate hand hygiene, which of the following equipment is necessary before examining this patient?

A. Facemask, non-sterile gloves, and gown
B. Respirator, sterile gloves, and gown
C. Nonsterile gloves and gown
D. Nonsterile gloves only
E. Sterile gloves and gown
F. Sterile gloves only

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A. Facemask, non-sterile gloves, and gown (19%)
B. Respirator, sterile gloves, and gown (4%)
C. Nonsterile gloves and gown (33%)
D. Nonsterile gloves only (11%)
E. Sterile gloves and gown (22%)
F. Sterile gloves only (9%)

Correct

33%
Answered correctly

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Time Spent

12/18/2020
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Contact precautions	
Organisms	• MDR organisms (eg, MRSA, VRE) • Enteric organisms (eg, *Clostridium difficile*) • Scabies
Infection-control measures	• Hand hygiene **(soap & water for *C difficile*)** • Nonsterile gloves • **Gown** • Private room preferred

MDR = multidrug-resistant; **MRSA** = methicillin-resistant *Staphylococcus aureus*; **VRE** = vancomycin-resistant *Enterococcus*.

This hospitalized patient's fever and diarrhea a few days after antibiotic initiation are concerning for ***Clostridium difficile*** infection. All hospitalized patients require **standard precautions**, including handwashing before and after patient contact, proper disposal of cleaning instruments and linens, and occasional use of gowns and gloves as required (eg, contact with body fluids).

However, cases of suspected or proven *C difficile* infection require additional **contact precautions**

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However, cases of suspected or proven *C difficile* infection require additional **contact precautions**, including handwashing with **soap and water** (alcohol-based hand sanitizers do **not** kill the spores), **gown** for **any** patient contact, and nonsterile **gloves** that should be changed after contact with contaminated secretions. Gloves alone would not be sufficient **(Choice D)**. In addition, a dedicated stethoscope and blood pressure cuff should be left in the patient's room.

(Choice A) Certain pathogens are transmitted by droplets (>5 microns) that remain suspended in air for limited periods only (eg, *Neisseria meningitides*, influenza, *Bordetella pertussis, Mycoplasma pneumoniae*, respiratory syncytial virus). In such cases, healthcare workers need to wear a simple facemask when within 6-10 feet of affected patients (droplet precautions). Gloves and gowns are not required.

(Choice B) Airborne precautions include an isolated room with negative pressure ventilation and a respirator mask with filtering capacity (eg, N95 mask) to avoid potential exposure to aerosolized particles (<5 microns) that can remain suspended in air for extended periods. Gloves and gowns are not needed. Airborne precautions are required for certain bacteria (eg, tuberculosis) and viruses (eg, varicella), but not for *C difficile*.

(Choices E and F) Sterile gloves generally are used for minor procedures or surgeries but are not required in patients with contact precautions.

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(Choices E and F) Sterile gloves generally are used for minor procedures or surgeries but are not required in patients with contact precautions.

Educational objective:

Clostridium difficile requires additional contact precautions, including handwashing with soap and water, a gown for any patient contact, and nonsterile gloves that should be changed after contact with contaminated secretions. Alcohol-based hand sanitizers do not kill the bacterial spores.

References

- Environmental interventions to control Clostridium difficile.

Microbiology	Infectious Diseases	Clostridium difficile infection
Subject	System	Topic

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A 6-year-old previously healthy girl is brought to the emergency department due to a day of fever, abdominal pain, and diarrhea. The symptoms began abruptly with high fever and cramping, periumbilical abdominal pain and were quickly followed by low-volume diarrhea mixed with blood and mucus. The patient has had no sick contacts and has not traveled recently; the family had dinner at a buffet restaurant 3 days ago. Temperature is 38.9 C (102 F). Physical examination reveals mild diffuse abdominal tenderness with no guarding or rebound tenderness. Bowel sounds are hyperactive. Stool occult blood testing is positive, and there are numerous leukocytes in the stool. Culture of the stool yields gram-negative, oxidase-positive, curved rods. Which of the following is the most likely pathogen responsible for this patient's symptoms?

A. *Campylobacter jejuni*
B. *Escherichia coli*
C. *Salmonella enterica*
D. *Shigella flexneri*
E. *Vibrio cholerae*

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abdominal pain, and diarrhea. The symptoms began abruptly with high fever and cramping, periumbilical abdominal pain and were quickly followed by low-volume diarrhea mixed with blood and mucus. The patient has had no sick contacts and has not traveled recently; the family had dinner at a buffet restaurant 3 days ago. Temperature is 38.9 C (102 F). Physical examination reveals mild diffuse abdominal tenderness with no guarding or rebound tenderness. Bowel sounds are hyperactive. Stool occult blood testing is positive, and there are numerous leukocytes in the stool. Culture of the stool yields gram-negative, oxidase-positive, curved rods. Which of the following is the most likely pathogen responsible for this patient's symptoms?

- ✓ A. *Campylobacter jejuni* (81%)
- B. ~~*Escherichia coli*~~ (3%)
- C. *Salmonella enterica* (4%)
- D. *Shigella flexneri* (5%)
- E. ~~*Vibrio cholerae*~~ (5%)

81% 01 min, 38 secs 02/11/2021

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Campylobacter jejuni	
Epidemiology	• Motile, curved, gram-negative rod • Leading cause of **foodborne gastroenteritis** • Transmission: contaminated food (undercooked **poultry**) & pets (dogs)
Manifestations	• Fever, abdominal pain, **watery diarrhea** ± bloody diarrhea • Self-limited in most cases; lasts ~7 days
Complications	• **Guillain-Barré** syndrome (cross-reacting antibody to myelin gangliosides)

Campylobacter jejuni is a motile, **oxidase-positive, curved, gram-negative rod** that is a leading cause of bacterial gastroenteritis in the United States. This pathogen resides in the gastrointestinal tract of a wide range of mammals and is transmitted via the fecal-oral route. Most cases arise when humans ingest contaminated food, particularly **undercooked poultry** or unpasteurized milk, but a minority of infections is caused by close contact with domesticated animals (eg, dogs, farm animals).

C jejuni is enteroinvasive and typically causes fever, abdominal pain, and **diarrhea** that may or may not be bloody. Stool studies usually reveal inflammation (blood, leukocytes); culture of the stool (enriched media

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caused by close contact with domesticated animals (eg, dogs, farm animals).

C jejuni is enteroinvasive and typically causes fever, abdominal pain, and **diarrhea** that may or may not be bloody. Stool studies usually reveal inflammation (blood, leukocytes); culture of the stool (enriched media at 42 C [107.6 F] and microaerophilic conditions) is diagnostic. Most cases are self-limited and resolve with supportive treatment within 5 days.

(Choice B) *Escherichia coli* causes many forms of gastroenteritis, including enterotoxin-mediated watery diarrhea (enterotoxigenic), Shiga toxin–mediated hemorrhagic colitis (enterohemorrhagic), and invasive colitis (enteroinvasive). Although this pathogen is a gram-negative enteric rod, it is oxidase-negative and not typically described as curved.

(Choice C) Non-typhoidal *Salmonella* (*S enterica*) is a common cause of bacterial gastroenteritis. This enteroinvasive pathogen frequently causes self-limited abdominal pain, fever, and watery diarrhea (bloody diarrhea is less common but can occur). However, *Salmonella* is oxidase-negative and not typically described as curved.

(Choice D) *Shigella* is a highly virulent bacterium that is often transmitted via the fecal-oral route in day care centers or other areas of communal habituation. It causes inflammatory colitis with fever; abdominal pain; and mucoid, bloody, and/or watery diarrhea. Shiga toxin, which irreversibly inhibits host cell protein synthesis, is a major virulence factor. However, *Shigella* is oxidase-negative and is not typically described

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described as curved.

(Choice D) *Shigella* is a highly virulent bacterium that is often transmitted via the fecal-oral route in day care centers or other areas of communal habituation. It causes inflammatory colitis with fever; abdominal pain; and mucoid, bloody, and/or watery diarrhea. Shiga toxin, which irreversibly inhibits host cell protein synthesis, is a major virulence factor. However, *Shigella* is oxidase-negative and is not typically described as curved.

(Choice E) *Vibrio cholerae* is also a curved, oxidase-positive, gram-negative enteric rod and can therefore occasionally be misidentified as a *Campylobacter* species. However, *V cholerae* causes massive watery diarrhea (due to cholera toxin) that is noninflammatory (no fecal leukocytes or erythrocytes).

Educational objective:
Campylobacter jejuni is an oxidase-positive, curved, gram-negative rod that is a leading cause of gastroenteritis. The pathogen is a zoonotic organism most commonly contracted by consuming contaminated, undercooked poultry. Cases are marked by fever, abdominal pain, and diarrhea that may be bloody.

Microbiology	Infectious Diseases	Acute diarrhea
Subject	System	Topic

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A 6-day-old boy is brought to the emergency department for inability to feed for 12 hours. His parents report that the infant has been unable to open his mouth and has held his hands clenched all day. The infant was delivered at home by the grandmother. The mother had no access to prenatal care but says that the pregnancy was uncomplicated. The mother immigrated to the United States 6 years ago. Physical examination shows increased muscle tone throughout, arching of the back, and dorsiflexed feet. The umbilical cord is covered with a clump of soil. The mother says that it is customary in her village where she grew up to cover the umbilical stump with dung to speed cord separation. In addition to hygienic umbilical cord care, which of the following is the most effective strategy to prevent this condition?

A. Early postpartum breastfeeding
B. Prophylactic antibiotics
C. Prophylactic immune globulin
D. Vaccination of infants at birth
E. Vaccination of pregnant women

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report that the infant has been unable to open his mouth and has held his hands clenched all day. The infant was delivered at home by the grandmother. The mother had no access to prenatal care but says that the pregnancy was uncomplicated. The mother immigrated to the United States 6 years ago. Physical examination shows increased muscle tone throughout, arching of the back, and dorsiflexed feet. The umbilical cord is covered with a clump of soil. The mother says that it is customary in her village where she grew up to cover the umbilical stump with dung to speed cord separation. In addition to hygienic umbilical cord care, which of the following is the most effective strategy to prevent this condition?

A. Early postpartum breastfeeding (3%)
B. Prophylactic antibiotics (5%)
C. Prophylactic immune globulin (17%)
D. Vaccination of infants at birth (17%)
✓ E. Vaccination of pregnant women (56%)

Correct
56%
30 secs
02/12/2021

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Neonatal tetanus	
Clinical features	• Difficulty feeding, **trismus** • Spasms & hypertonicity ◦ Clenched hands, dorsiflexed feet, **opisthotonus** • Eventual respiratory failure
Treatment	• Supportive care • Antibiotics & tetanus immune globulin
Prevention	• Immunization of pregnant women & those of childbearing age • Hygienic delivery & cord care

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Neonatal tetanus (tetanus neonatorum) is a major cause of infant mortality in developing countries but is rare in the United States. Neonatal tetanus results from the introduction of *Clostridium tetani* spores to the infant, generally from **unhygienic deliveries or cord care**. **Symptoms** typically begin **5-7 days after birth** and can progress more rapidly than in adults. Infected infants become irritable and have **difficulty feeding** and suckling due to tonic spasm of the masticatory muscles (trismus). As the disease progresses,

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infant, generally from **unhygienic deliveries or cord care**. **Symptoms** typically begin **5-7 days after birth** and can progress more rapidly than in adults. Infected infants become irritable and have **difficulty feeding** and suckling due to tonic spasm of the masticatory muscles (trismus). As the disease progresses, **spasms and hypertonicity** become more generalized. Mortality approaches 100% without treatment.

Prevention of neonatal tetanus focuses on **vaccinating women** who are pregnant or may become pregnant with inactivated tetanus toxin (tetanus toxoid). Appropriately vaccinated women provide **transplacental IgG** to the fetus, which decreases the incidence of neonatal tetanus by approximately 95%.

(Choice A) Secretory IgA found in breast milk helps prevent respiratory and gastrointestinal infections in the newborn by providing mucosal immune support. However, adequate protection against neonatal tetanus requires the presence of toxin-neutralizing, circulating IgG antibodies that are obtained transplacentally.

(Choices B and C) Treatment of tetanus, including neonatal tetanus, involves the use of antibiotics to kill *C tetani* and administration of tetanus immune globulin to neutralize unbound toxin. However, these agents are not used for tetanus prevention.

(Choice D) Tetanus vaccination is not given at birth because the neonatal immune system is immature and unable to mount a proper memory immune response against the tetanus toxoid. The first dose of the

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transplacentally.

(Choices B and C) Treatment of tetanus, including neonatal tetanus, involves the use of antibiotics to kill *C tetani* and administration of tetanus immune globulin to neutralize unbound toxin. However, these agents are not used for tetanus prevention.

(Choice D) Tetanus vaccination is not given at birth because the neonatal immune system is immature and unable to mount a proper memory immune response against the tetanus toxoid. The first dose of the diphtheria-pertussis-tetanus series is commonly administered at 2 months of age. In areas of endemic tetanus disease, this vaccine can be given as early as 4-6 weeks of age, but not earlier.

Educational objective:

Neonatal tetanus can be prevented by hygienic delivery and umbilical cord care and universal immunization of women who are pregnant or may become pregnant. Immunized mothers provide passive immunity via transplacental IgG, protecting infants until they receive active immunization (vaccination) around age 2 months.

References

- Maternal and neonatal tetanus.

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www.ncbi.nlm.nih.gov/pubmed/25149223

A 26-year-old man is brought to the emergency department due to fever and lethargy. His girlfriend says the patient abruptly began experiencing fever, chills, vomiting, and diarrhea several hours ago, which were quickly followed by lightheadedness and lethargy. He has no prior medical conditions other than an episode of epistaxis after a bar fight 3 days ago. The patient does not smoke cigarettes or use injection drugs. There is no history of exposure to sick contacts, and he has not eaten anything out of the ordinary. Temperature is 38.9 C (102 F), blood pressure is 90/60 mm Hg, and pulse is 120/min. Physical examination shows a diffuse, erythematous rash. There is an anterior nasal packing in the left nostril, removal of which shows mild mucosal erythema with a purulent discharge. Cardiopulmonary and abdominal examinations reveal no abnormalities, and signs of meningeal irritation are absent. Which of the following processes is most essential in pathogenesis of this patient's current condition?

A. Activation of toll-like receptors by bacterial components
B. Binding of T-cell receptors by bacterial secretory products
C. Bridging of cell-bound IgE by multivalent antigens
D. Phagocytosis of bacteria in the blood by neutrophils
E. Presentation of processed antigens by dendritic cells

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A. Activation of toll-like receptors by bacterial components (24%)

✓ B. Binding of T-cell receptors by bacterial secretory products (55%)

C. Bridging of cell-bound IgE by multivalent antigens (3%)

D. Phagocytosis of bacteria in the blood by neutrophils (8%)

E. Presentation of processed antigens by dendritic cells (6%)

Correct

55%

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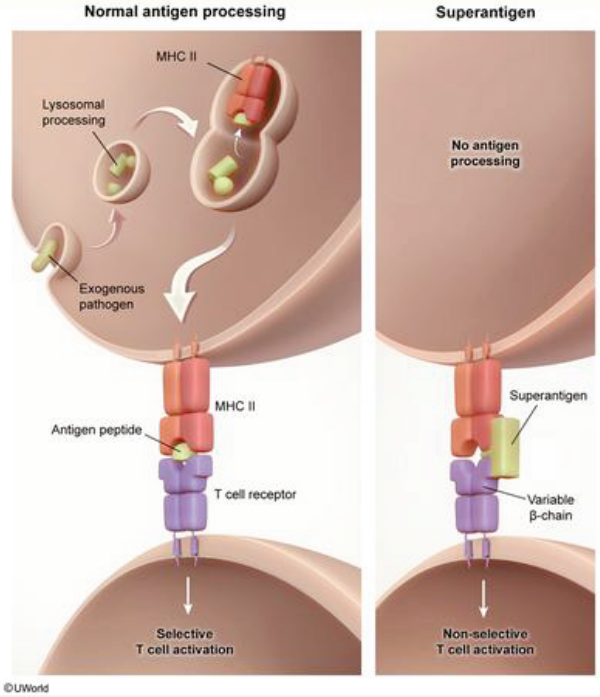
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Staphylococcal toxic shock syndrome (TSS) is an exotoxin-mediated disease associated with rapid-onset high fever, hypotension, multiorgan failure, and a diffuse, erythematous rash. Most cases are linked to prolonged tampon use or **nasal wound packing**, which provides a medium for localized *Staphylococcus aureus* proliferation and the elaboration of **pyrogenic toxin superantigens** (eg, toxic shock syndrome toxin-1 [TSST-1]) into the bloodstream.

Pyrogenic toxin superantigens are generated by strains of *S aureus* (and *Streptococcus pyogenes*) that have acquired an underlying mobile genetic element via bacteriophage or plasmid. These exotoxins are called superantigens because they bind to the invariant region of the MHC-II complex of antigen-presenting cells without first being internalized and processed (MHC-II antigens are normally processed by the phagolysosome) **(Choice E)**. The superantigen/MHC-II complex subsequently interacts with the variable part of the T-cell receptor beta chain, which results in the **nonspecific stimulation** of a large percentage (>20%) of total **T cells** and the massive release of inflammatory cytokines (eg, IL-1, IL-2, TNF-alpha & beta, interferon-gamma). Cytokine release mediates the major manifestations of TSS including fever, increased capillary permeability, and hypotension.

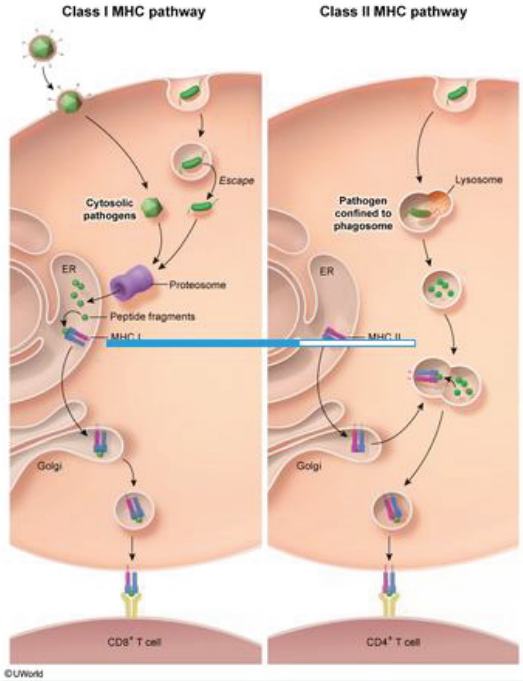
(Choice A) Endotoxin in the cell membrane of gram-negative bacteria can cause rapid-onset fever and

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increased capillary permeability, and hypotension.

(Choice A) Endotoxin in the cell membrane of gram-negative bacteria can cause rapid-onset fever and hypotension due to activation of toll-like receptors on cells of the innate immune system. However, in this case, the presence of nasal packing and a diffuse, erythematous rash make TSS far more likely than gram-negative sepsis.

(Choice C) Anaphylactic shock occurs due to antigen-stimulated cross-linking of IgE that is bound to basophils or mast cells, which activates the cell and releases massive amounts of inflammatory mediators. Anaphylactic shock is typically characterized by hypotension, bronchospasm, and shortness of breath; most cases are triggered by insect stings, food, or medications, and manifestations occur shortly after exposure.

(Choice D) Patients who develop TSS usually have a noninvasive infection in the vaginal canal or area of wound packing. TSS is mediated by the absorption of superantigens into the blood, not the invasion of bacteria.

Educational objective:

Toxic shock syndrome is typically associated with the prolonged use of tampons or wound packing, which allows *Staphylococcus aureus* to replicate locally and release pyrogenic toxic superantigens (eg, toxic

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(Choice C) Anaphylactic shock occurs due to antigen-stimulated cross-linking of IgE that is bound to basophils or mast cells, which activates the cell and releases massive amounts of inflammatory mediators. Anaphylactic shock is typically characterized by hypotension, bronchospasm, and shortness of breath; most cases are triggered by insect stings, food, or medications, and manifestations occur shortly after exposure.

(Choice D) Patients who develop TSS usually have a noninvasive infection in the vaginal canal or area of wound packing. TSS is mediated by the absorption of superantigens into the blood, not the invasion of bacteria.

Educational objective:

Toxic shock syndrome is typically associated with the prolonged use of tampons or wound packing, which allows *Staphylococcus aureus* to replicate locally and release pyrogenic toxic superantigens (eg, toxic shock syndrome toxin-1) into the blood. Superantigens bind to the MHC-II complex of antigen-presenting cells without processing and nonspecifically activate T cells. This leads to a dramatic release of inflammatory cytokines, which causes the manifestations of the disease (eg, hypotension; high fever; organ failure; diffuse, erythematous rash).

References

- Exotoxins of Staphylococcus aureus

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A 37-year-old woman comes to the office due to right-sided abdominal discomfort that has been getting progressively worse over the past few weeks. She has not had any nausea or vomiting. The patient's family moved to the United States from rural Kazakhstan when she was a child. The patient has no drug allergies. She does not use tobacco or alcohol. She has a dog at home. Temperature is 36.7 C (98.1 F). Physical examination is notable for hepatomegaly. Ultrasound reveals a large liver mass with cystic lesions. During surgery to resect the mass, the patient suffers from a procedural complication and dies. At the family's request, an autopsy is performed. A cut section of a portion of the mass is shown in the image below.



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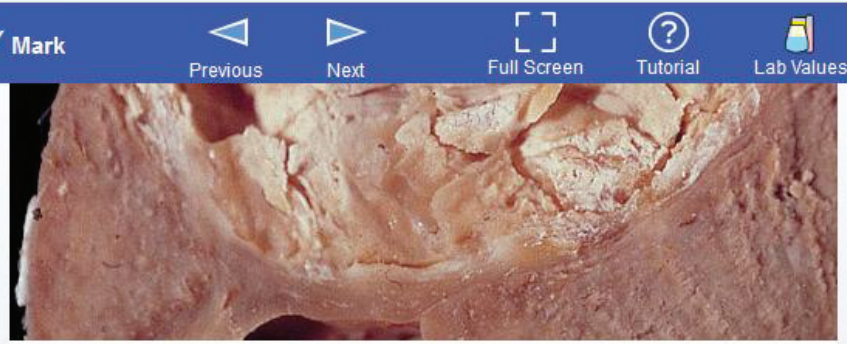
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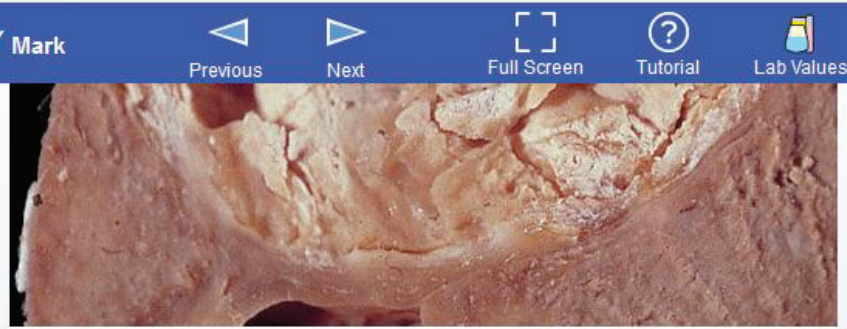
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Which of the following is the most likely cause of this patient's death?

A. Anaphylaxis
B. Fulminant liver failure
C. Hypovolemia
D. Pulmonary embolism
E. Septic shock

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Which of the following is the most likely cause of this patient's death?

- A. Anaphylaxis (48%)
- B. Fulminant liver failure (12%)
- C. Hypovolemia (6%)
- D. Pulmonary embolism (15%)
- E. Septic shock (17%)

Correct

48%

59 secs

12/20/2020

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The tapeworm ***Echinococcus granulosus*** is the most common cause of **hydatid cysts**. Most cases occur in individuals from endemic regions (eg, eastern Mediterranean, Middle East, South America, sub-Saharan Africa, former Soviet Union, western China) or those residing in the southwestern United States with **sheep** and **dog** (participate in the tapeworm life cycle) exposure. Initial infection is generally asymptomatic, with subsequent manifestations depending on cyst location and size. The **liver** is often affected (leading to hepatomegaly or right upper quadrant pain), but other organs such as the lungs or muscles can be involved. Unilocular lesions are typical of *E granulosus*, and multilocular lesions are typical of *E multilocularis*.

When infection occurs, echinococcal larvae implant within the capillaries, triggering an inflammatory reaction involving monocytes and eosinophils. Some larvae encyst. Microscopic examination demonstrates an encapsulated and calcified cyst ("**eggshell calcification**") containing fluid and budding cells that will eventually become daughter cysts. The outer wall is composed of gelatinous sheets surrounded by a thick fibrous capsule. Imaging (ultrasound, CT, MRI) and serology testing can be used for diagnosis.

Depending on the size of the cyst, surgery and adjunctive chemotherapy (eg, albendazole) are the treatment of choice for symptomatic patients. Cyst manipulation (eg, surgery, aspiration) should be

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Depending on the size of the cyst, surgery and adjunctive chemotherapy (eg, albendazole) are the treatment of choice for symptomatic patients. Cyst manipulation (eg, surgery, aspiration) should be performed with caution, as spilling of cyst contents can cause **anaphylactic shock**, which likely occurred in this patient.

(Choices B, C, D, and E) Fulminant liver failure can arise due to numerous conditions, including viral hepatitis, acetaminophen toxicity, idiosyncratic drug reactions, or Wilson disease. Hypovolemia is typically caused by severe blood loss, although excessive loss of other bodily fluids (eg, diarrhea, vomiting, burns, dehydration) may also be responsible. Pulmonary emboli are typically caused by the propagation of venous thrombi, with less common sources including air bubbles, fat droplets, amniotic fluid, or clumps of parasites or malignant cells. Overwhelming systemic infection with bacterial organisms can cause septic shock (hypotension, low blood flow). None of these conditions is typically associated with hydatid cysts.

Educational objective:
Echinococcus granulosus is the most common cause of hydatid cysts. Spilling of cyst contents can cause anaphylactic shock. Surgical manipulation should be performed with caution.

Pathophysiology Infectious Diseases Echinococcosis

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A 26-year-old man comes to the office due to 2 days of rash on his right thigh. It is mildly pruritic and not painful. He has no chronic medical conditions but occasionally takes ibuprofen for shoulder pain following intensive workouts at the gym. Temperature is 37.2 C (98.6 F), blood pressure is 115/78 mm Hg, and pulse is 94/min. The rash is shown in the image below:



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No other lesions are seen. Which of the following is the most likely underlying cause of this patient's rash?

A. Drug-induced cytotoxic T-cell activation

B. Fungal infection due to shared gym equipment

C. Type 1 hypersensitivity reaction to an insect bite

D. Spread of spirochetes through the dermis

E. Spread of *Streptococcus* through lymphatic channels

Submit

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No other lesions are seen. Which of the following is the most likely underlying cause of this patient's rash?

A. Drug-induced cytotoxic T-cell activation (6%)

B. Fungal infection due to shared gym equipment (7%)

C. Type 1 hypersensitivity reaction to an insect bite (17%)

✓ D. Spread of spirochetes through the dermis (68%)

E. Spread of *Streptococcus* through lymphatic channels (0%)

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Explanation

This patient's annular, erythematous rash with central clearing suggests **erythema migrans** (EM), the hallmark feature of early localized **Lyme disease**. Lyme disease is caused by the spirochete *Borrelia burgdorferi* and is transmitted by the *Ixodes scapularis* tick during blood feeding. *B burgdorferi* replicates at the site of inoculation, which generates a rash 7-14 days after transmission in most patients.

EM typically begins as a confluent macule that expands outward as *B burgdorferi* **spreads through the dermis**. Most cases evolve over days into an **annular lesion with central clearing**, which resembles a **bull's-eye**. Pain is rare, and pruritis is typically mild or absent. However, some patients have systemic manifestations (eg, malaise, fever, headache). Because many patients with Lyme disease do not recall a tick bite, suspicion for Lyme disease should be raised in any individual from an endemic area who develops a characteristic EM rash.

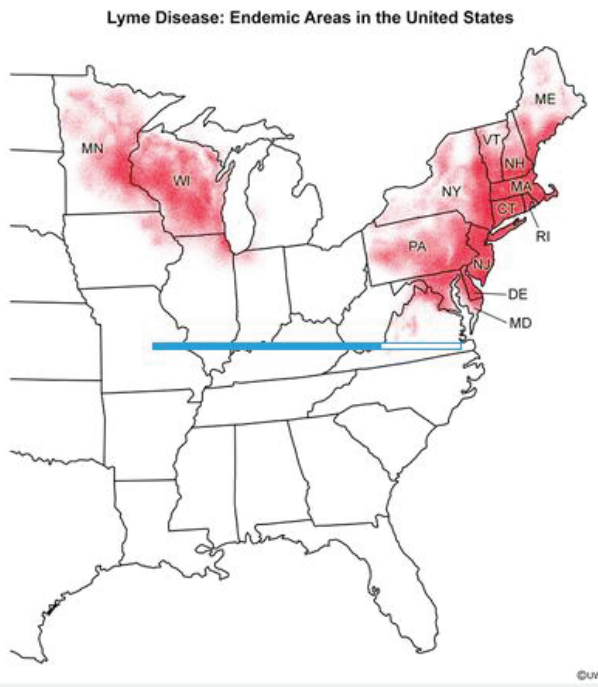
(Choice A) Nonsteroidal anti-inflammatory drugs (eg, ibuprofen) can sometimes cause a fixed drug reaction, which is marked by the activation of cytotoxic T cells in a particular location within the dermis. Although patients frequently develop an annular rash, it is usually a dusky red plaque with no central clearing.

(Choice B) Tinea corporis can sometimes be spread through contact with fomites (eg, gym equipment).

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Explanation

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[Choice B] Tinea corporis can sometimes be spread through contact with fomites (eg, gym equipment).

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[Choice B] Tinea corporis can sometimes be spread through contact with fomites (eg, gym equipment).

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(Choice B) Tinea corporis can sometimes be spread through contact with fomites (eg, gym equipment). Although this fungal infection often causes an annular lesion with central clearing that spreads outward, the advancing edge has raised borders, and the lesions are usually intensely pruritic.

(Choice C) A type 1 hypersensitivity (allergic) reaction to an insect bite usually arises within minutes and is marked by an edematous lesion that is intensely pruritic. This patient with 2 days of progressive rash that is nonpruritic is unlikely to be experiencing an allergic reaction.

(Choice E) *Streptococcal* lymphangitis is marked by the formation of erythematous streaks up the lymphatic channel. The formation of an annular lesion with central clearing would be atypical.

Educational objective:

Lyme disease should be suspected in any individual from an endemic area who develops erythema migrans, a slowly expanding annular lesion with central clearing (bull's-eye rash). Most cases are not pruritic or painful, but patients sometimes have systemic symptoms (eg, fever, myalgia, headache).

References

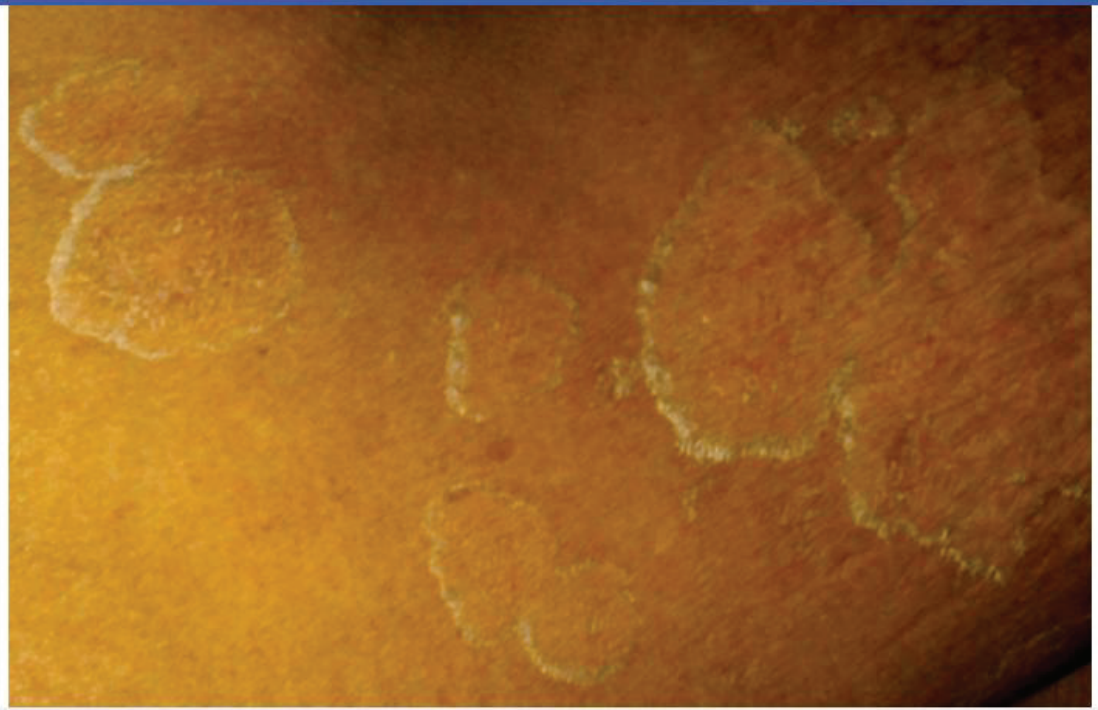
- Erythema migrans.

Pathology Infectious Diseases Lyme disease

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A 43-year-old male with advanced HIV is hospitalized for evaluation of recent-onset headaches and personality changes. Imaging of the brain shows a solitary mass within the temporal lobe. Biopsy of the mass reveals uniform cells containing the Epstein-Barr virus genome. This patient most likely suffers from which of the following?

- A. Pilocytic astrocytoma
- B. Glioblastoma
- C. Oligodendroglioma
- D. Ependymoma
- E. Medulloblastoma
- F. Primary CNS lymphoma
- G. Meningioma
- H. Craniopharyngioma
- I. Schwannoma

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which of the following?

- A. Pilocytic astrocytoma
- B. Glioblastoma
- C. Oligodendroglioma
- D. Ependymoma
- E. Medulloblastoma
- F. Primary CNS lymphoma
- G. Meningioma
- H. Craniopharyngioma
- I. Schwannoma
- J. Pituitary adenoma

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which of the following?

- A. Pilocytic astrocytoma (1%)
- B. Glioblastoma (4%)
- C. Oligodendroglioma (2%)
- D. Ependymoma (1%)
- E. Medulloblastoma (1%)
- ✓ F. Primary CNS lymphoma (80%)
- G. Meningioma (2%)
- H. Craniopharyngioma (2%)
- I. Schwannoma (1%)
- J. Pituitary adenoma (0%)

80% 41 secs 10/20/2020

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The most frequent CNS tumor in immunosuppressed patients is a primary CNS lymphoma. This CNS tumor is commonly associated with AIDS.

Primary CNS lymphomas appear microscopically as dense, cellular aggregates of uniform, atypical lymphoid cells. The majority of primary CNS lymphomas arise from B-cells. Diffuse large B-cell lymphoma is the most common subtype. The cells of CNS lymphomas are commonly positive for the B-cell markers CD20 and CD79a.

Primary CNS lymphomas are universally associated with the Epstein-Barr virus (EBV). The clinical presentation is non-specific. Mental status changes, seizures, or progressive focal neurologic deficits may occur. Most of CNS lymphomas are high-grade and respond poorly to chemotherapy.

(Choice G) Meningiomas are not associated with immunosuppressive diseases, nor are they associated with EBV. Meningiomas are located adjacent to the brain surface and are attached to the dura mater.

(Choice H) Craniopharyngiomas are located in the suprasellar region and can be calcified. Craniopharyngiomas can cause visual disturbances and endocrinopathies (such as hypopituitarism).

(Choice I) Intracranial schwannomas are most commonly located at the cerebellopontine angle. They cause symptoms of CN VIII compression (hearing loss, tinnitus, loss of balance)

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(Choice I) Intracranial schwannomas are most commonly located at the cerebellopontine angle. They cause symptoms of CN VIII compression (hearing loss, tinnitus, loss of balance).

Educational Objective:
Primary CNS lymphomas occur in immunosuppressed patients, such as those suffering from AIDS. These tumors arise from B cells and are universally associated with EBV. They are high-grade tumors with a poor prognosis.

Pathology	Infectious Diseases	Cns lymphoma
Subject	System	Topic

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A 20-year-old woman comes to the urgent care center due to 3 days of vaginal pain with intercourse and dysuria. She also had low-grade fevers and a mild headache. The patient is otherwise healthy and takes oral contraceptives only. She has no history of urinary tract infections or sexually transmitted infections. She is sexually active and recently began a monogamous relationship with a new partner. Her boyfriend uses condoms inconsistently. On examination, she is afebrile. She is uncomfortable, but in no acute distress. Her abdomen is soft and nontender. Genital examination reveals multiple, painful, shallow ulcers with an erythematous base on the left labia. There is no vaginal discharge. Internal examination reveals no cervical motion tenderness. She has bilateral tender inguinal lymphadenopathy. Which of the following is the best diagnostic test for this patient's condition?

A. Darkfield microscopy
B. Gram stain of the ulcer swab
C. Lymph node biopsy
D. Polymerase chain reaction for viral DNA
E. Potassium hydroxide preparation

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oral contraceptives only. She has no history of urinary tract infections or sexually transmitted infections. She is sexually active and recently began a monogamous relationship with a new partner. Her boyfriend uses condoms inconsistently. On examination, she is afebrile. She is uncomfortable, but in no acute distress. Her abdomen is soft and nontender. Genital examination reveals multiple, painful, shallow ulcers with an erythematous base on the left labia. There is no vaginal discharge. Internal examination reveals no cervical motion tenderness. She has bilateral tender inguinal lymphadenopathy. Which of the following is the best diagnostic test for this patient's condition?

A. Darkfield microscopy (10%)

B. Gram stain of the ulcer swab (18%)

C. Lymph node biopsy (3%)

D. Polymerase chain reaction for viral DNA (65%)

E. ~~Potassium hydroxide preparation~~ (2%)

Correct

65%

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Genital ulcer disease				
	Syphilis	**Genital herpes**	**Chancroid**	**Granuloma inguinale (donovanosis)**
Causative agent	*Treponema pallidum*	Herpes simplex virus	*Haemophilus ducreyi*	*Klebsiella granulomatis*
Description	Single, **painless** ulcer at inoculation site with heaped-up borders & clean base	Multiple, **painfulsuperficialvesicles** or **ulcerations** with erythematous base	**Deep**, **purulent**, painful ulcers with matted/**suppurative** lymphadenitis	**Painless**, progressive, red serpiginous ulcerative lesions **without** lymphadenopathy
				• Gram stain &

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Diagnostic tests	• VDRL/RPR • Dark-field microscopy	• PCR • Tzanck smear	• Gram stain & culture • PCR	• Gram stain & culture (difficult) • Biopsy (Donovan bodies)

PCR = polymerase chain reaction; **RPR** = rapid plasma reagin; **VDRL** = Venereal Disease Research Laboratory.

Primary genital **herpes simplex virus (HSV)** infection is the most likely diagnosis in this patient who has **multiple painful** genital ulcers (with a characteristic erythematous base), dysuria (likely due to irritation from the ulcers), tender lymphadenopathy (common with primary genital HSV infection), and **systemic** symptoms (fever, headache) in the setting of having a new sexual partner. The characteristic **vesicles** are often **absent**. HSV infection can be diagnosed using polymerase chain reaction (PCR), direct fluorescence antibody, viral culture (low sensitivity), or Tzanck smear (showing multinucleated giant cells).

(Choice A) Darkfield microscopy can be used to diagnose syphilis, which typically presents with painless ulcerations (chancre).

(Choice B) Gonorrhea, caused by *Neisseria gonorrhoeae*, is a common cause of urethritis, cervicitis, and

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(Choice A) Darkfield microscopy can be used to diagnose syphilis, which typically presents with painless ulcerations (chancre).

(Choice B) Gonorrhea, caused by *Neisseria gonorrhoeae*, is a common cause of urethritis, cervicitis, and pelvic inflammatory disease in sexually active females. Gram stain can reveal gram-negative diplococci. Chancroid (due to *Haemophilus ducreyi*) presents with purulent ulcers with "ragged" borders and suppurative lymphadenopathy. Gram stain may occasionally reveal gram-negative rods in a "school of fish" chain.

(Choice C) Lymph node biopsy is a relatively invasive procedure typically used to exclude malignancy or certain infections such as tuberculosis. Biopsies of genital lesions may be performed if the diagnosis is unclear or if there is no response to initial treatment.

(Choice E) Potassium hydroxide testing can be used to identify *Candida* infections, including vulvovaginitis. However, this condition typically presents with a white discharge, not genital ulcers.

Educational objective:
The finding of multiple painful genital ulcers and constitutional symptoms in a sexually active patient is highly suggestive of primary genital herpes simplex virus infection. Diagnosis can be established by polymerase chain reaction testing, direct fluorescence antibody testing, viral culture, or Tzanck smear.

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A 24-year-old hospital phlebotomist comes to the occupational health clinic after sustaining a needlestick injury while drawing blood from a hepatitis B–positive patient. She has no medical history and received the complete hepatitis B vaccination series prior to her hospital employment a year ago. She is closely monitored over the next 6 months with repeat hepatitis B serologies and does not develop clinical or laboratory evidence of infection. Which of the following mechanisms most likely explains her immunity?

A. Activated $CD8^+$ T-lymphocyte–mediated clearance
B. Disrupted replication of the viral genome
C. Expression of interferon from infected cells
D. Impaired virion entry into hepatocytes
E. Reduced assembly of virions within the cytosol

Submit

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A 24-year-old hospital phlebotomist comes to the occupational health clinic after sustaining a needlestick injury while drawing blood from a hepatitis B–positive patient. She has no medical history and received the complete hepatitis B vaccination series prior to her hospital employment a year ago. She is closely monitored over the next 6 months with repeat hepatitis B serologies and does not develop clinical or laboratory evidence of infection. Which of the following mechanisms most likely explains her immunity?

A. ~~Activated CD8+ T-lymphocyte–mediated clearance~~ (42%)
B. Disrupted replication of the viral genome (4%)
C. ~~Expression of interferon from infected cells~~ (3%)
✓ D. Impaired virion entry into hepatocytes (47%)
E. ~~Reduced assembly of virions within the cytosol~~ (1%)

Correct

47%
Answered correctly

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Time Spent

02/15/2021
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Serologic evidence of **hepatitis B virus** (HBV) exposure is present in approximately 2 billion people worldwide. Nearly 250 million of these individuals have chronic infection and can transmit the virus to others. Perinatal transmission is most common in high prevalence countries (eg, sub-Saharan Africa); unprotected sex or intravenous drug use causes most infections in low-incidence countries (eg, United States). **Health care providers** are at **high risk** for infection due to potential exposure to the blood of infected patients.

HBV **vaccination** is recommended for all health care providers and other high-risk individuals (eg, intravenous drug users). The vaccine utilizes **recombinant HBsAg** to generate protective immunity against the virus. HBsAg is a collection of envelope glycoproteins found on the surface of HBV; these glycoproteins mediate attachment of the virus to hepatocytes and subsequent viral entry. Patients who adequately respond to the HBV vaccine generate **anti-HBs antibodies**, which bind to circulating viral particles and prevent attachment to and penetration of hepatocytes.

Patients who have been immunized against HBV as well as those who have cleared the virus after acute infection will have anti-HBs antibodies. These 2 populations are distinguished by the presence of anti-HBc antibodies, which are seen only in those who have been exposed to the virus (not in immunized patients).

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(Choice A) The immunity conferred by the hepatitis B vaccination is mediated by protective antibodies against HBsAg; the protective effects are not due to activation of cytotoxic T cells. However, in patients exposed to HBV, the resolution of acute infection is mediated primarily by a vigorous, polyclonal cytotoxic T-cell response that destroys infected hepatocytes.

(Choice B) HIV treatment often includes nucleotide and non-nucleoside reverse transcriptase inhibitors, which disrupt viral genome replication. Hepatitis C virus is often treated with similar medications (eg, sofosbuvir) that target viral RNA-dependent RNA polymerase. Immunization against HBV does not interfere with replication of the HBV genome.

(Choice C) HBV is considered a stealth virus because it possesses virulence factors that block portions of the innate immune system, including the release of interferon-gamma from infected cells. However, HBV immunization does not significantly affect the innate immune system.

(Choice E) NS5A inhibitors (eg, ledipasvir) are thought to block hepatitis C virus replication and assembly. HBV immunization generates protective antibodies against the HBsAg; it does not affect viral assembly.

Educational objective:
Immunization against hepatitis B virus uses recombinant HBsAg to generate anti-HBs antibodies. These antibodies prevent infection by binding to the envelope of circulating virus and inhibiting viral entry.

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(Choice B) HIV treatment often includes nucleotide and non-nucleoside reverse transcriptase inhibitors, which disrupt viral genome replication. Hepatitis C virus is often treated with similar medications (eg, sofosbuvir) that target viral RNA-dependent RNA polymerase. Immunization against HBV does not interfere with replication of the HBV genome.

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(Choice E) NS5A inhibitors (eg, ledipasvir) are thought to block hepatitis C virus replication and assembly. HBV immunization generates protective antibodies against the HBsAg; it does not affect viral assembly.

Educational objective:
Immunization against hepatitis B virus uses recombinant HBsAg to generate anti-HBs antibodies. These antibodies prevent infection by binding to the envelope of circulating virus and inhibiting viral entry.

References

- Novel mechanism of antibodies to hepatitis B virus in blocking viral particle release from cells.
- Hepatitis B: the virus and disease.

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A 21-year-old man comes to the emergency department due to shortness of breath, fatigue, myalgias, and debilitating retroorbital headaches for the past several days. The patient is on summer break and came to work at his grandparents' dairy farm 3 weeks ago. He cleans out animal waste from the barn, but he does not handle hay. His past medical history is insignificant. He does not use tobacco or illicit drugs. The patient's temperature is 38.8 C (101.8 F). Bronchial breath sounds are heard in the right lower lung. There are no cardiac murmurs. Abdominal examination is unremarkable. Chest x-ray demonstrates right lower and middle lobe consolidation. Laboratory results are as follows:

Complete blood count	
Hemoglobin	14 g/dL
Platelets	60,000/mm^3
Leukocytes	8,800/mm^3
Liver function studies	
Aspartate aminotransferase (SGOT)	162 U/L

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Liver function studies

Aspartate aminotransferase (SGOT)	162 U/L
Alanine aminotransferase (SGPT)	174 U/L

An HIV test is negative.

Which of the following is the most likely cause of this patient's symptoms?

A. *Borrelia burgdorferi*
B. *Coxiella burnetii*
C. Epstein Barr virus
D. *Escherichia coli*
E. *Salmonella enterica*

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Aspartate aminotransferase (SGOT)	162 U/L
Alanine aminotransferase (SGPT)	174 U/L

An HIV test is negative.

Which of the following is the most likely cause of this patient's symptoms?

- A. *Borrelia burgdorferi* (7%)
- ✓ B. *Coxiella burnetii* (85%)
- C. ~~Epstein Barr virus~~ (2%)
- D. ~~*Escherichia coli*~~ (1%)
- E. ~~*Salmonella enterica*~~ (3%)

Correct

85%

01 min, 59 secs

01/18/2021

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Q fever is a zoonosis caused by ***Coxiella burnetii***. Human infection usually occurs through inhalation of bacteria from air contaminated by **animal waste**. Q fever has acute and chronic stages. **Acute** Q fever manifests as a nonspecific febrile illness with fever lasting >10 days, fatigue, and myalgias. Severe debilitating **headaches**, which are often **retroorbital** and associated with photophobia, are a frequent symptom. **Pneumonia** is one of the primary signs of acute Q fever, and the most common x-ray abnormality is lobar consolidation. Leukocyte count is often normal. Other classic laboratory findings are increased liver enzymes and **thrombocytopenia**. Chronic Q fever, which is frequently fatal if not treated, is rare, may occur in patients with or without previous symptomatic acute infection, and manifests as infective endocarditis in patients with valvular disease.

(Choice A) *Borrelia burgdorferi* is a spirochete that is the causative agent in Lyme disease, transmitted to humans through the bite of the *Ixodes* tick. Manifestations include erythema migrans (target lesion), febrile illness with headaches and joint pains, and central nervous system or cardiac involvement. Pneumonia would be unusual.

(Choice C) Epstein-Barr virus causes infectious mononucleosis (malaise, pharyngitis, splenomegaly).

(Choice D) *Escherichia coli* can infect the udders of cows and cause infection of unpasteurized milk, but it is unlikely to cause a febrile illness with retroorbital headaches and pneumonia.

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would be unusual.

(Choice C) Epstein-Barr virus causes infectious mononucleosis (malaise, pharyngitis, splenomegaly).

(Choice D) *Escherichia coli* can infect the udders of cows and cause infection of unpasteurized milk, but it is unlikely to cause a febrile illness with retroorbital headaches and pneumonia.

(Choice E) Salmonellosis typically causes a gastrointestinal illness with abdominal cramps and diarrhea.

Educational objective:

Q fever is a zoonotic infection that occurs in farm workers exposed to waste from cattle and sheep. Its causative agent is *Coxiella burnetii*. A patient with exposure to waste from farm animals who develops a nonspecific illness (myalgias, fatigue, fever [>10 days], retroorbital headache) with a normal leukocyte count, thrombocytopenia, and increased liver enzymes should be evaluated for acute Q fever infection.

References

- Diagnosis and management of Q fever — United States, 2013: recommendations from CDC and the Q Fever Working Group.

Microbiology	Infectious Diseases	Q fever
Subject	System	Topic

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A 34-year-old man comes to the physician due to fever, myalgias, malaise, and progressive fatigue over a 2-week period. He has not experienced any sore throat. He recently received a blood transfusion while hospitalized for a bleeding duodenal ulcer. Physical examination shows mild splenomegaly. There is no lymphadenopathy and no jaundice. Lymphocytosis is identified in the peripheral blood with 30% atypical lymphocytes. The patient's serum fails to agglutinate horse erythrocytes. The agglutination test is repeated a week later and, again, no agglutination is noted. HIV testing is negative. Which of the following is the most likely cause of this patient's condition?

A. Coxsackievirus A
B. Cytomegalovirus
C. Epstein-Barr virus
D. Hepatitis C virus
E. JC virus
F. Parvovirus B19

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2-week period. He has not experienced any sore throat. He recently received a blood transfusion while hospitalized for a bleeding duodenal ulcer. Physical examination shows mild splenomegaly. There is no lymphadenopathy and no jaundice. Lymphocytosis is identified in the peripheral blood with 30% atypical lymphocytes. The patient's serum fails to agglutinate horse erythrocytes. The agglutination test is repeated a week later and, again, no agglutination is noted. HIV testing is negative. Which of the following is the most likely cause of this patient's condition?

- A. Coxsackievirus A (2%)
- ✓ B. Cytomegalovirus (62%)
- ✗ C. Epstein-Barr virus (15%)
- D. Hepatitis C virus (8%)
- E. JC virus (3%)
- F. Parvovirus B19 (6%)

Incorrect
Correct answer

62%
Answered correctly

01 min, 20 secs
Time Spent

03/12/2021
Last Updated

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Most cases of **infectious mononucleosis (IM)**, caused by the **Epstein-Barr virus (EBV)**, are associated with **serum heterophile antibodies** that agglutinate with erythrocytes from unrelated species (eg, horse erythrocytes in the Monospot test, sheep erythrocytes in the classic Paul-Bunnell test). The agglutination test may be negative at the beginning of the infection and can be repeated later for confirmation. Because the Monospot (horse erythrocyte agglutination) test was negative on 2 separate occasions in this patient with a mononucleosis-like syndrome (fever, fatigue, splenomegaly, atypical lymphocytosis), his symptoms are **unlikely** to be due to EBV; the lack of sore throat and lymphadenopathy is also atypical for classic EBV-associated IM **(Choice C)**.

In immunocompetent patients with a **heterophile antibody-negative mononucleosis-like syndrome**, the most likely diagnosis is **cytomegalovirus (CMV) infection**. Pharyngitis and lymphadenopathy are seen less commonly than with EBV. CMV can be acquired during the transfusion of leukocyte-laden blood products, as the virus infects leukocytes of granulocyte-macrophage lineage. Irradiation helps reduce this risk. Other causes of heterophile antibody-negative mononucleosis-like syndromes include human herpesvirus-6, HIV, and toxoplasmosis.

(Choice A) Coxsackie A viruses cause aseptic meningitis and herpangina (fever, posterior pharyngeal gray vesicles/ulcers) in children.

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(Choice A) Coxsackie A viruses cause aseptic meningitis and herpangina (fever, posterior pharyngeal gray vesicles/ulcers) in children.

(Choice D) Acute hepatitis C (HCV) rarely causes symptoms. Transfusion-acquired HCV can cause chronic hepatitis, but highly sensitive blood donor screening tests have led to low transmission rates. Atypical lymphocytosis is less common with HCV than with EBV or CMV.

(Choice E) JC virus causes progressive multifocal leukoencephalopathy (PML), a central nervous system viral infection seen in immunocompromised patients. Clinical manifestations include hemiparesis, visual field defects (eg, hemianopsia), and cognitive impairment.

(Choice F) Parvovirus B19 causes erythema infectiosum, a childhood illness characterized by red, flushed cheeks ("slapped cheeks" appearance). The virus can also cause aplastic crises in patients with sickle cell anemia and hydrops fetalis in the fetus.

Educational objective:
The Monospot test is positive in most cases of Epstein-Barr virus-associated mononucleosis. In immunocompetent patients with a heterophile antibody-negative mononucleosis-like syndrome, the most likely diagnosis is cytomegalovirus infection.

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A 59-year-old woman is brought to the emergency department with fever, skin flushing, and an altered level of consciousness. Her blood pressure is 50/20 mmHg, and her heart rate is 120/min despite receiving IV fluids. If blood cultures are positive for *E. coli*, which of the following bacterial factors is most directly responsible for this patient's current condition?

- A. Capsule
- B. Fimbrial antigen
- C. Heat-stable exotoxin
- D. Lipid A
- E. O antigen

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A 59-year-old woman is brought to the emergency department with fever, skin flushing, and an altered level of consciousness. Her blood pressure is 50/20 mmHg, and her heart rate is 120/min despite receiving IV fluids. If blood cultures are positive for *E. coli*, which of the following bacterial factors is most directly responsible for this patient's current condition?

A. Capsule (14%)
B. Fimbrial antigen (9%)
C. Heat-stable exotoxin (12%)
D. Lipid A (51%)
E. O antigen (10%)

Correct

51%
Answered correctly

49 secs
Time Spent

10/05/2020
Last Updated

Explanation

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This patient has **septic shock** (ie, fluid-refractory hypotension in a patient with sepsis) as a result of the release of **bacterial endotoxins** into the bloodstream. Endotoxins are found in the outer membrane of Gram-negative bacteria (eg, *E. coli*), which is composed of lipopolysaccharide (LPS). LPS is released by destruction of the bacterial cell wall or during cell division. LPS is a very long, heat-stable molecule arranged into three regions: O antigen, core polysaccharide, and Lipid A.

Lipid A is toxic to mammalian cells and acts as a virulence factor by inducing the release of endogenous pyrogens (eg, IL-1, prostaglandins) and inflammatory mediators (eg, TNFa, interferon) from activated macrophages. These cytokines cause the manifestations of septic shock: fever, **hypotension**, increased vascular permeability with third-spacing of fluids, and **organ failure**.

(Choice A) *E. coli* strains can produce a capsule (eg, K-1 antigen) which provides a defense against phagocytosis by immune cells but does not directly contribute to the manifestations of septic shock.

(Choice B) Fimbriae, or pili, allow bacteria to adhere to the target tissue and establish infection. Although Enterotoxigenic *E. coli* is an example of an organism that uses fimbriae, bacterial adhesion is not directly responsible for the manifestations of septic shock.

(Choice C) Heat-stable exotoxin is one of the enterotoxins produced by Enterotoxigenic *E. coli* but is responsible for secretory diarrhea rather than the manifestations of septic shock.

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Exhibit Display

Escherichia coli virulence factors		
Virulence factor	**Mechanism**	**Presentation**
Lipopolysaccharide	Macrophage activation causes widespread release of IL-1, IL-6 & TNF-α	Bacteriemia & septic shock
K1 capsular polysaccharide	Prevents phagocytosis & complement-mediated lysis	Neonatal meningitis
Verotoxin (shiga-like toxin)	Inactivates the 60S ribosomal component, halting protein synthesis & causing cell death	Gastroenteritis (bloody)
Heat-stable/heat-labile enterotoxins	Promotes fluid & electrolyte secretion from intestinal epithelium	Gastroenteritis (watery)
P fimbriae	Allows adhesion to uroepithelium	Urinary tract infections

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27

A 6-year-old boy whose family recently immigrated to the United States is brought to the office due to sore throat and fever. Examination shows mild tonsillar erythema with exudates. A sample from the exudates is obtained. On microscopic evaluation, there are clumped, gram-positive bacteria with polar granules that stain deeply with aniline dyes. Which of the following best explains the pathogenicity of the organism most likely responsible for this patient's condition?

A. Activation of electrolyte transport
B. Blockade of neurotransmitter release
C. Cellular membrane disruption
D. Impairment of protein synthesis
E. Widespread T cell activation

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A 6-year-old boy whose family recently immigrated to the United States is brought to the office due to sore throat and fever. Examination shows mild tonsillar erythema with exudates. A sample from the exudates is obtained. On microscopic evaluation, there are clumped, gram-positive bacteria with polar granules that stain deeply with aniline dyes. Which of the following best explains the pathogenicity of the organism most likely responsible for this patient's condition?

- A. ~~Activation of electrolyte transport~~ (2%)
- B. ~~Blockade of neurotransmitter release~~ (2%)
- C. Cellular membrane disruption (19%)
- ✓ D. Impairment of protein synthesis (67%)
- E. ~~Widespread T cell activation~~ (9%)

Correct

67% Answered correctly

01 min, 53 secs Time Spent

02/26/2021 Last Updated

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Diphtheria

Epidemiology	• Endemic in developing countries due to inadequate vaccination but rare in developed countries
Microbiology/ pathogenesis	• ***Corynebacterium diphtheriae*** colonize respiratory tract & secrete diphtheria toxin, the primary virulence factor • **Diphtheria toxin** is an AB exotoxin that inhibits protein synthesis by ADP-ribosylation of EF-2 • Toxin acts locally, causing respiratory cell necrosis with formation of fibrinous, coagulative exudates
Clinical symptoms	• Sore throat • Fever • Cervical adenopathy • Pharyngeal exudates/**coalescing pseudomembrane**
Complications	• Submucosal edema & pseudomembrane aspiration can obstruct respiratory tract, causing **suffocation** • Systemically absorbed diphtheria toxin has predilection for brain & heart tissue ○ **Myocarditis/heart failure** ○ **Neurologic toxicity**

EF-2 = elongation factor 2

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Corynebacterium diphtheriae are nonmotile, unencapsulated, gram-positive rods. On microscopic examination, they are often found in clumps (classically said to resemble Chinese characters) or joined in V- or Y-shaped chains. Their cytoplasm contains metachromatic **granules** that stain with **aniline** dyes (eg, methylene blue).

C diphtheriae produce classic 2-subunit **AB exotoxin**. The B (binding) subunit binds specifically to the heparin-binding epidermal growth factor receptor on cardiac and neural cells, which explains the toxin's affinity for heart and brain tissue. The B subunit induces endocytosis of the toxin, and the subsequently released A (active) subunit inhibits host cell protein synthesis by catalyzing the ADP-ribosylation of protein elongation factor 2 (EF-2). EF-2 is necessary for tRNA to insert new amino acids into the growing protein chain during translation. Therefore, the toxin causes cell death by inhibiting cell protein synthesis.

(Choice A) Certain virulent enteric bacteria (eg, *Campylobacter jejuni, Vibrio cholerae*) release AB exotoxins that activate electrolyte transport. These toxins have 5 B subunits responsible for cell binding and toxin endocytosis and 1 A subunit that stimulates a G protein to increase intracellular cAMP concentrations. As a result, active efflux of sodium and chloride ions occurs, and the subsequent cell water loss into the gut lumen leads to watery diarrhea and dehydration.

(Choice B) Botulinum toxin is a neurotoxin that blocks exocytosis of acetylcholine-containing presynaptic

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loss into the gut lumen leads to watery diarrhea and dehydration.

(Choice B) Botulinum toxin is a neurotoxin that blocks exocytosis of acetylcholine-containing presynaptic vesicles from peripheral nerve terminals, causing cranial and peripheral nerve palsies, muscle weakness, and respiratory paralysis. Tetanus toxin inhibits the release of the inhibitory neurotransmitters gamma-aminobutyric acid and glycine. Classic manifestations of tetanus include muscle spasms and autonomic hyperactivity.

(Choice C) *Clostridium perfringens* releases a cytolytic toxin (alpha-toxin, or phospholipase C) that degrades cell membrane phospholipids, causing cell destruction.

(Choice E) Superantigens (eg, staphylococcal and streptococcal toxic shock toxins) bind nonspecifically to T cell receptors and major histocompatibility complex class II molecules on antigen-presenting cells, leading to widespread T cell stimulation and inflammation. However, they are classically implicated in toxic shock syndrome related to tampon use or nasal packing, not upper respiratory infections.

Educational objective:
Diphtheria exotoxin inhibits host cell protein synthesis by catalyzing the ADP-ribosylation of host cell elongation factor-2.

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A 34-year-old man comes to the emergency department due to recurrent fevers, chills, and excessive sweating. The symptoms began a few days ago and seem to occur every 48 hours. The patient recently returned from a trip to India. Temperature is 38.6 C (101.5 F). Physical examination is otherwise unrevealing. Laboratory studies are notable for anemia and thrombocytopenia. A blood smear with Giemsa staining demonstrates red blood cell inclusions. The patient is prescribed chloroquine and primaquine. The addition of primaquine to the treatment regimen is most likely to have which of the following effects?

A. Decrease the side effects of chloroquine therapy
B. Kill blood trophozoites
C. Prevent disease relapse
D. Prevent hemolysis
E. Treat chloroquine-resistant strains

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A 34-year-old man comes to the emergency department due to recurrent fevers, chills, and excessive sweating. The symptoms began a few days ago and seem to occur every 48 hours. The patient recently returned from a trip to India. Temperature is 38.6 C (101.5 F). Physical examination is otherwise unrevealing. Laboratory studies are notable for anemia and thrombocytopenia. A blood smear with Giemsa staining demonstrates red blood cell inclusions. The patient is prescribed chloroquine and primaquine. The addition of primaquine to the treatment regimen is most likely to have which of the following effects?

A. ~~Decrease the side effects of chloroquine therapy~~ (1%)
B. Kill blood trophozoites (16%)
C. Prevent disease relapse (46%)
D. ~~Prevent hemolysis~~ (2%)
E. Treat chloroquine-resistant strains (32%)

Incorrect

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This patient has fever, chills, sweats, and red blood cell inclusions on Giemsa smear that developed following travel to a tropical geographic region (areas including South America, Africa, India, and Southeast Asia). Together, these findings support a diagnosis of **malaria**. Fever and sweating that occur every 48 hours (tertian malaria) are especially characteristic of *Plasmodium vivax, P ovale*, or *P falciparum* infection.

All species of malaria-causing organisms share a similar life cycle. Organisms are first inoculated into the human host by the ***Anopheles*** mosquito and then travel to the **liver**, where they infect hepatocytes and replicate. Lysis of infected hepatocytes releases **merozoites** into the bloodstream. Merozoites go on to infect erythrocytes, and it is the resultant erythrocyte lysis that causes relapsing fevers and sweating. ***P vivax* and *P ovale*** are unique in that they also establish a **latent** hepatic infection (exo-erythrocytic cycle) in the form of **hypnozoites**, responsible for **relapses**.

Chloroquine is effective in eradicating chloroquine-sensitive plasmodia from the bloodstream, but it has no activity against the latent hepatic infections established by *P vivax* and *P ovale*. **Primaquine** must be added to the regimen to completely eradicate the **hypnozoites**.

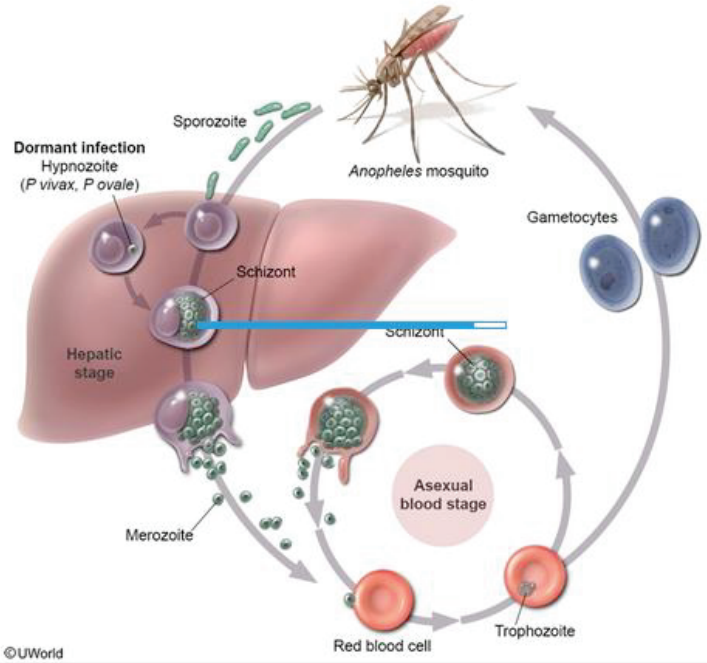
(Choice A) Retinopathy is the most serious long-term adverse effect related to chloroquine use. It occurs only rarely and is related to prolonged use. Primaquine has no influence on the occurrence of chloroquine

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Exhibit Display

Malaria life cycle



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added to the regimen to completely eradicate the **hypnozoites**.

(Choice A) Retinopathy is the most serious long-term adverse effect related to chloroquine use. It occurs only rarely and is related to prolonged use. Primaquine has no influence on the occurrence of chloroquine retinopathy.

(Choices B and E) Primaquine has limited therapeutic activity against the erythrocytic forms of plasmodia, including trophozoites. Primaquine is not effective in treating chloroquine-resistant strains, which can be managed with mefloquine or quinine, among others.

(Choice D) No antimalarial agent specifically acts to prevent hemolysis. Primaquine is contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency as the medication can cause hemolysis.

Educational objective:
Chloroquine is the treatment of choice for uncomplicated malaria contracted in a chloroquine-sensitive geographic region. It eliminates susceptible erythrocytic forms of all *Plasmodium* species. Primaquine is added in the treatment of infections with *P vivax* and *P ovale* to eradicate the intrahepatic stages (hypnozoites) of these malarial species, which are responsible for relapses.

Pharmacology	Infectious Diseases	Malaria
Subject	System	Topic

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A 24-year-old man comes to the emergency department due to bloody diarrhea. His symptoms began 10 days ago with episodic abdominal discomfort and loose stools. The symptoms have progressively worsened, and he has had 6–8 stools mixed with blood and mucus over the past 2 days. The patient recently returned from a 2-week trip to Egypt and felt well while traveling. Temperature is 38 C (100.4 F), blood pressure is 120/70 mm Hg, and pulse is 86/min. The abdomen is soft with mild tenderness on palpation of lower quadrants. There is no guarding or rebound tenderness, and bowel sounds are hyperactive. Stool testing is negative for *C difficile* toxin, and stool culture yields no bacteria. Sigmoidoscopy reveals colonic ulcers with undermining edges that contain trophozoites. The causative organism for this patient's current condition can also produce which of the following manifestations?

A. Bile duct obstruction
B. Cystic brain lesions
C. Granulomatous cystitis
D. Itchy cutaneous eruptions
E. Liver abscess

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days ago with episodic abdominal discomfort and loose stools. The symptoms have progressively worsened, and he has had 6–8 stools mixed with blood and mucus over the past 2 days. The patient recently returned from a 2-week trip to Egypt and felt well while traveling. Temperature is 38 C (100.4 F), blood pressure is 120/70 mm Hg, and pulse is 86/min. The abdomen is soft with mild tenderness on palpation of lower quadrants. There is no guarding or rebound tenderness, and bowel sounds are hyperactive. Stool testing is negative for *C difficile* toxin, and stool culture yields no bacteria. Sigmoidoscopy reveals colonic ulcers with undermining edges that contain trophozoites. The causative organism for this patient's current condition can also produce which of the following manifestations?

A. Bile duct obstruction (6%)
B. Cystic brain lesions (3%)
C. Granulomatous cystitis (5%)
D. Itchy cutaneous eruptions (3%)
E. Liver abscess (80%)

80%
01 min, 41 secs
11/17/2020

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Entamoeba histolytica	
Risk factors	• Amoeba transmitted via the fecal-oral route • Ingestion of contaminated food/water • **Developing nations** (travel/residence)
Manifestations	• 90% of patients asymptomatic • **Colitis** (diarrhea, bloody stool with mucus, abdominal pain) • **Liver abscess** (RUQ pain, fever) • Brain, lung, pleura abscess (less common)
Diagnosis	• Stool ova & parasites – **trophozoites/cysts** • Colonoscopy – **flask-shaped** colonic ulcers

RUQ = right upper quadrant.

Entamoeba histolytica is an amoeba that infects the gastrointestinal tract of humans and is transmitted via the fecal-oral route when cysts are ingested from contaminated food or water. Cases are rare in the United States but commonly occur in developing regions where sanitation is poor. Most infected patients

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Entamoeba histolytica is an amoeba that infects the gastrointestinal tract of humans and is transmitted via the fecal-oral route when cysts are ingested from contaminated food or water. Cases are rare in the United States but commonly occur in developing regions where sanitation is poor. Most infected patients have no symptoms, but a minority (~10%) develop clinically significant **colitis** with subacute bloody-mucoid diarrhea, abdominal pain, and fever. The diagnosis is confirmed when **cysts and trophozoites** are seen on stool studies and/or colonic visualization demonstrates **flask-shaped colonic ulcers** (with trophozoites).

Colonic *E histolytica* infections occasionally (~1%) spread through the bloodstream to the liver, lungs, and/or brain. The most common extraintestinal manifestation is a single **amebic liver abscess** in the right lobe of the liver. Invasive strains are more likely to have amebic proteases that degrade host extracellular membranes and secretory IgA. Almost all invasive strains also demonstrate **contact-dependent cytotoxicity**, whereby an amebic lectin binds the host cell, introduces an amebic porin into the host cell membrane, and causes cell lysis.

(Choice A) Liver flukes (eg, *Clonorchis*, *Opisthorchis*) are typically transmitted due to consuming contaminated fish. The pathogen can remain in the bile duct of an infected patient for decades. Many cases are asymptomatic, but complications such as bile duct obstruction can occur.

(Choice B) Ingestion of the egg stage of the pork tapeworm *Taenia solium* leads to neurocysticercosis

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(Choice B) Ingestion of the egg stage of the pork tapeworm *Taenia solium* leads to neurocysticercosis, which is characterized by the formation of cystic brain lesions. Manifestations often occur years later and include seizures (primarily) and focal neurologic signs. Spread of *E histolytic* to the brain would cause an abscess, not a cyst.

(Choice C) Schistosomiasis is parasitic blood fluke infection that is acquired when bathing or swimming in freshwater that contains the intermediate host, a freshwater snail. Most cases are asymptomatic but urinary shedding of eggs through the bladder can result in granulomatous inflammation, ulcerations, and, ultimately, bladder cancer.

(Choice D) Cutaneous larva migrans is a hookworm infection that causes an intensely itchy, reddish-brown, migrating, serpiginous cutaneous track in the area near penetration (usually the lower extremities).

Educational objective:
Entamoeba histolytica is an amoeba that causes colitis characterized by ulcers with undermining edges (ie, flask-shaped) that may contain cysts and trophozoites. Trophozoites can occasionally (~1%) invade the colonic wall and disseminate through the blood to the liver, brain, or lungs. Amebic hepatic abscess is the most common extraintestinal manifestation.

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An 83-year-old woman is brought to the emergency department from a nursing home with fever and altered mental status. The patient has a history of hypertension, dementia, and fecal incontinence. Her temperature is 38.3 C (100.9 F), blood pressure is 100/68 mm Hg, and pulse is 114/min. She is lethargic and unable to answer questions. Her abdomen is soft, with suprapubic tenderness. Lungs are clear bilaterally. There is no cardiac murmur or skin rash. Laboratory results are as follows:

Blood	
Leukocytes	17,000/mm^3
Potassium	3.8 mEq/L
Bicarbonate	22 mEq/L
Creatinine	0.8 mg/dL
Urinalysis	
Leukocyte esterase	positive

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Urinalysis	
Leukocyte esterase	positive
Nitrites	positive
Leukocytes	10/hpf

A chest x-ray reveals normal-appearing lungs. Blood and urine cultures are performed, and empiric antibiotics are initiated. Urine cultures grow gram-negative rods that are lactose-fermenting and indole-positive. Which of the following is the most likely organism causing this patient's infection?

A. *Enterobacter cloacae*
B. *Escherichia coli*
C. *Haemophilus influenzae*
D. *Proteus mirabilis*
E. *Pseudomonas aeruginosa*

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esterase

Nitrites	positive
Leukocytes	10/hpf

A chest x-ray reveals normal-appearing lungs. Blood and urine cultures are performed, and empiric antibiotics are initiated. Urine cultures grow gram-negative rods that are lactose-fermenting and indole-positive. Which of the following is the most likely organism causing this patient's infection?

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C. *Haemophilus influenzae*
D. *Proteus mirabilis*
E. *Pseudomonas aeruginosa*

Submit

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esterase	
Nitrites	positive
Leukocytes	10/hpf

A chest x-ray reveals normal-appearing lungs. Blood and urine cultures are performed, and empiric antibiotics are initiated. Urine cultures grow gram-negative rods that are lactose-fermenting and indole-positive. Which of the following is the most likely organism causing this patient's infection?

A. *Enterobacter cloacae* (6%)
B. *Escherichia coli* (83%)
C. *Haemophilus influenzae* (0%)
D. *Proteus mirabilis* (6%)
E. *Pseudomonas aeruginosa* (2%)

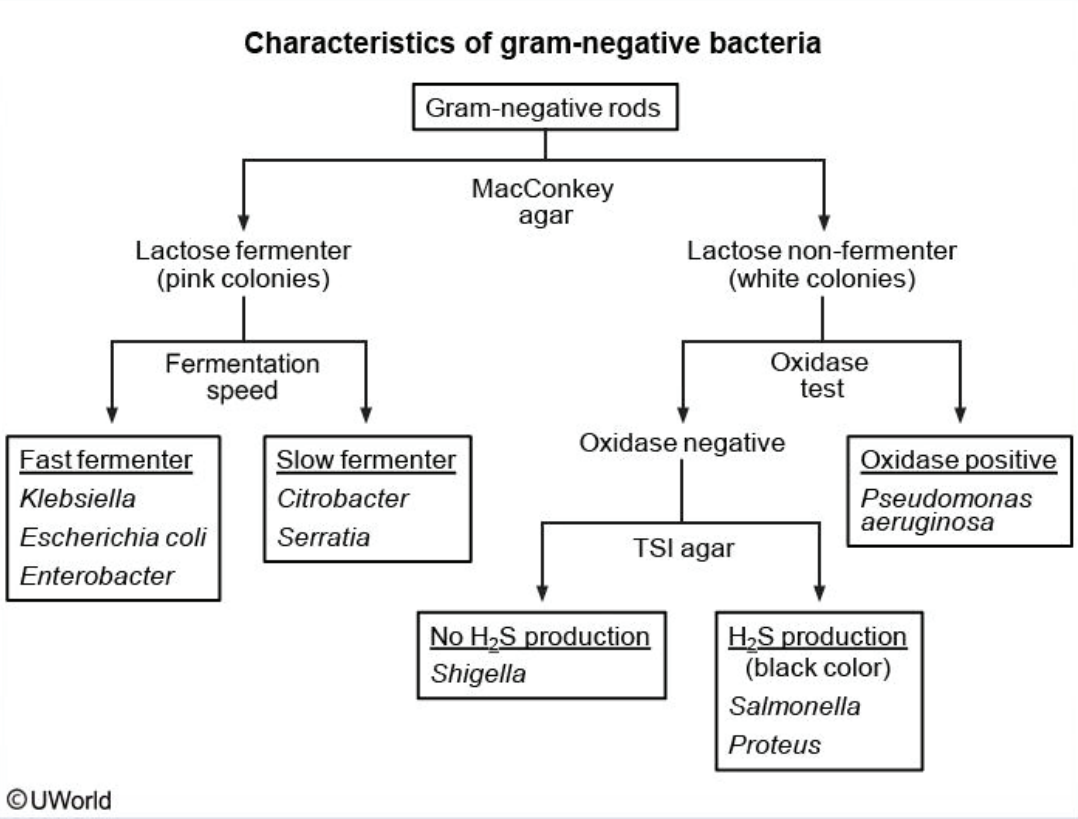
Correct

83%

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10/27/2020

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This patient has sepsis, most likely due to a **urinary tract infection** (UTI), as evidenced by the presence of pyuria (leukocytes), leukocyte esterase, and gram-negative rods in the urine. Among the organisms listed, the microbiological features - **lactose-fermenting, indole-positive gram-negative rods** - are characteristic of ***Escherichia coli***, the most common etiology of UTIs among elderly women. The indole positivity (ability to convert tryptophan to indole) of *E coli* distinguishes it from *Enterobacter cloacae*, another lactose-fermenting gram-negative rod that is a common cause of UTIs in women **(Choice A).** Both *E coli* and *E cloacae* are fast lactose fermenters.

(Choice C) *Haemophilus influenzae* are gram-negative organisms that colonize the respiratory tract rather than the gastrointestinal and genitourinary tracts; they do not typically cause UTIs. These organisms are frequent causes of pneumonia, sinusitis, and, less commonly, meningitis.

(Choices D and E) *Proteus mirabilis* and *Pseudomonas aeruginosa* are gram-negative organisms that can cause UTI, most commonly in patients with Foley catheters. However, in contrast to *E coli*, these organisms are lactose non-fermenters (do not form pink colonies on MacConkey agar).

Educational objective:
Escherichia coli are lactose-fermenting, indole-positive gram-negative rods that are an important cause of urinary tract infection in women.

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pyuria (leukocytes), leukocyte esterase, and gram-negative rods in the urine. Among the organisms listed, the microbiological features - **lactose-fermenting, indole-positive gram-negative rods** - are characteristic of ***Escherichia coli***, the most common etiology of UTIs among elderly women. The indole positivity (ability to convert tryptophan to indole) of *E coli* distinguishes it from *Enterobacter cloacae*, another lactose-fermenting gram-negative rod that is a common cause of UTIs in women **(Choice A).** Both *E coli* and *E cloacae* are fast lactose fermenters.

(Choice C) *Haemophilus influenzae* are gram-negative organisms that colonize the respiratory tract rather than the gastrointestinal and genitourinary tracts; they do not typically cause UTIs. These organisms are frequent causes of pneumonia, sinusitis, and, less commonly, meningitis.

(Choices D and E) *Proteus mirabilis* and *Pseudomonas aeruginosa* are gram-negative organisms that can cause UTI, most commonly in patients with Foley catheters. However, in contrast to *E coli*, these organisms are lactose non-fermenters (do not form pink colonies on MacConkey agar).

Educational objective:
Escherichia coli are lactose-fermenting, indole-positive gram-negative rods that are an important cause of urinary tract infection in women.

References

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A 33-year-old homeless man is hospitalized due to recent weight loss, odynophagia, and progressive cough. He is found to be HIV-positive and his CD4 count is 45/mm^3. The patient's condition improves on a newly instituted treatment, but 4 weeks later at outpatient follow-up he is found to have significantly elevated fasting blood glucose. Which of the following medications is most likely responsible for his hyperglycemia?

- A. Acyclovir
- B. Lopinavir
- C. Azithromycin
- D. Foscarnet
- E. Trimethoprim-sulfamethoxazole
- F. Zidovudine

Submit

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A 33-year-old homeless man is hospitalized due to recent weight loss, odynophagia, and progressive cough. He is found to be HIV-positive and his CD4 count is 45/mm^3. The patient's condition improves on a newly instituted treatment, but 4 weeks later at outpatient follow-up he is found to have significantly elevated fasting blood glucose. Which of the following medications is most likely responsible for his hyperglycemia?

A. ~~Acyclovir~~ (3%)
B. Lopinavir (45%)
C. ~~Azithromycin~~ (5%)
D. ~~Foscarnet~~ (13%)
E. ~~Trimethoprim-sulfamethoxazole~~ (8%)
F. Zidovudine (23%)

Correct

45%
Answered correctly

01 min, 18 secs
Time Spent

02/25/2021
Last Updated

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Mechanism of action of HIV antiretroviral medications		
Class	**Example(s)**	**Mechanism of action**
NRTI	Tenofovir, emtricitabine, lamivudine, abacavir, zidovudine	Inhibits HIV DNA synthesis from RNA template by terminating DNA chain elongation • NRTI: **Competitive** nucleoside/nucleotide RT inhibitor • NNRTI: **Allosteric** RT inhibitor
NNRTI	Efa**vir**enz, ne**vir**apine	
PI	Ataza**navir**, daru**navir**, indi**navir**, rito**navir**	Inhibits HIV polyprotein **cleavage**
Integrase inhibitor	Dolute**gravir**, ralte**gravir**	Inhibits HIV DNA integration into host genome
Fusion inhibitor	En**fu**virtide	Inhibits HIV fusion with target cell membrane by binding to HIV **gp41**
CCR5	Maraviroc	Inhibits HIV entry by blocking the HIV **gp120allosteric**

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inhibitor	Enfuvirtide	binding to HIV **gp41**
CCR5 antagonist	Maraviroc	Inhibits HIV entry by blocking the HIV **gp120allosteric** interaction with CCR5 (tropism testing required)

CCR5 = chemokine (C-C motif) receptor 5; **NNRTI** = non-nucleoside reverse transcriptase inhibitor; **NRTI** = nucleoside/nucleotide reverse transcriptase inhibitor; **PI** = protease inhibitor; **RT** = reverse transcriptase.

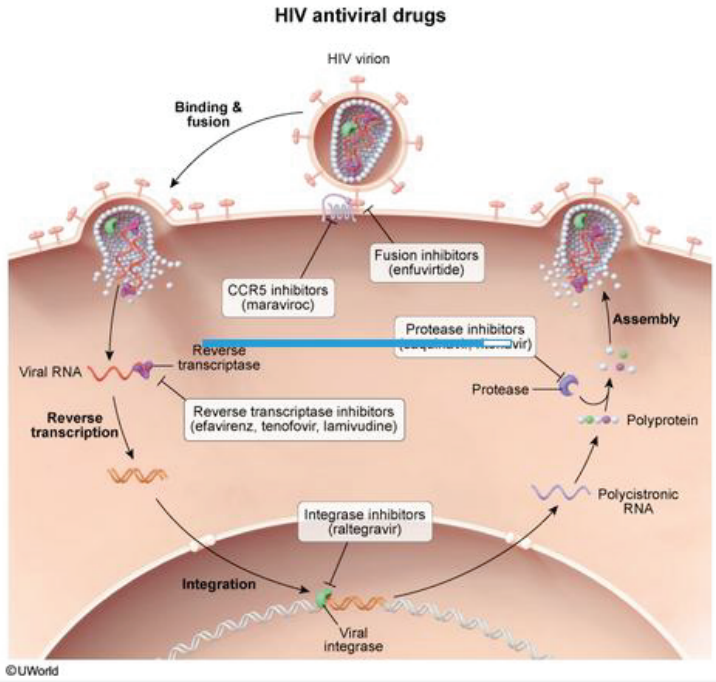
Lopinavir is a **protease inhibitor (PI)**. These drugs reversibly inhibit viral protease, an enzyme responsible for HIV polyprotein cleavage to form mature viral proteins. PIs are never used as monotherapy as viral resistance to the entire class can form quickly. The following important adverse effects can be seen with PIs:

1. **Lipodystrophy** leads to increased fat deposition on the back and abdomen and decreased adipose tissue on the face, extremities, and buttocks. This gives patients a "buffalo hump" appearance with central obesity and peripheral wasting.
2. **Hyperglycemia** results from increased insulin resistance and may lead to diabetes.
3. **Inhibition of cytochrome P450** may cause interactions with other drugs. Rifampin increases P450 activity and will therefore decrease PI serum levels; as a result, rifampin can be replaced with rifabutin

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Enfuvirtide

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activity and will therefore decrease PI serum levels; as a result, rifampin can be replaced with rifabutin

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2. **Hyperglycemia** results from increased insulin resistance and may lead to diabetes.
3. **Inhibition of cytochrome P450** may cause interactions with other drugs. Rifampin increases P450 activity and will therefore decrease PI serum levels; as a result, rifampin can be replaced with rifabutin in the treatment of tuberculosis in patients on PIs.

(Choice A) Acyclovir is an antiviral drug active against herpes simplex virus types 1 and 2 and varicella-zoster viruses. Renal toxicity is the most important side effect.

(Choice C) Azithromycin is a macrolide antibiotic used for treatment and prophylaxis of *Mycobacterium avium* complex infections in patients with HIV.

(Choice D) Foscarnet is used for the treatment of cytomegalovirus infections. It may cause nephrotoxicity and electrolyte disturbances (eg, hypocalcemia, hypomagnesemia, hypokalemia).

(Choice E) Trimethoprim-sulfamethoxazole (TMP-SMX) is used in patients with HIV for the prevention and treatment of pneumonia caused by *Pneumocystis jirovecii* (formerly *P carinii*). The most important side effects associated with TMP-SMX are megaloblastic anemia, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

(Choice F) Zidovudine is a nucleoside reverse transcriptase inhibitor (NRTI). NRTIs act by suppressing DNA synthesis from viral RNA. One of the most common side effects of zidovudine is bone marrow

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and electrolyte disturbances (eg, hypocalcemia, hypomagnesemia, hypokalemia).

(Choice E) Trimethoprim-sulfamethoxazole (TMP-SMX) is used in patients with HIV for the prevention and treatment of pneumonia caused by *Pneumocystis jirovecii* (formerly *P carinii*). The most important side effects associated with TMP-SMX are megaloblastic anemia, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

(Choice F) Zidovudine is a nucleoside reverse transcriptase inhibitor (NRTI). NRTIs act by suppressing DNA synthesis from viral RNA. One of the most common side effects of zidovudine is bone marrow toxicity, resulting in anemia in up to 40% of patients.

Educational objective:
Protease inhibitors are HIV antiretroviral medications that inhibit cleavage of the polypeptide precursor into mature viral proteins. Their side effects as a class include hyperglycemia, lipodystrophy, and drug-drug interactions due to inhibition of cytochrome P450.

Pharmacology	Infectious Diseases	Antiretroviral therapy
Subject	System	Topic

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A 35-year-old woman comes to the office due to a vulvar lesion. She has also experienced occasional headaches and memory loss recently. The patient has had unprotected sexual intercourse with multiple partners. Cardiovascular examination is notable for a diastolic murmur with a prominent second heart sound. There is a painless indurated nodule on her vulva. Cervical cultures are negative for gonorrhea, but a serum Venereal Disease Research Laboratory (VDRL) test is positive. Chest x-ray reveals calcifications at the level of the ascending aortic arch. Blood cultures are negative. Lumbar puncture shows mild pleocytosis and a positive VDRL result. HIV testing is negative. Which of the following best describes this patient's vulvar lesion?

A. Chancre
B. Condylomata acuminata
C. Condylomata lata
D. Granuloma inguinale
E. Gumma

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headaches and memory loss recently. The patient has had unprotected sexual intercourse with multiple partners. Cardiovascular examination is notable for a diastolic murmur with a prominent second heart sound. There is a painless indurated nodule on her vulva. Cervical cultures are negative for gonorrhea, but a serum Venereal Disease Research Laboratory (VDRL) test is positive. Chest x-ray reveals calcifications at the level of the ascending aortic arch. Blood cultures are negative. Lumbar puncture shows mild pleocytosis and a positive VDRL result. HIV testing is negative. Which of the following best describes this patient's vulvar lesion?

A. Chancre (28%)
B. Condylomata acuminata (4%)
C. Condylomata lata (23%)
D. Granuloma inguinale (1%)
E. Gumma (42%)

Correct

42%

01 min, 30 secs

01/18/2021

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This patient with neurosyphilis (headaches, memory loss, cerebrospinal fluid with Venereal Disease Research Laboratory positivity, pleocytosis) likely has cardiovascular syphilis (asymptomatic murmur with loud second heart sound [S2], ascending aortic arch calcification). She therefore has **late (tertiary) syphilis**, and her vulvar lesion is most likely a **gumma**. A chancre would be seen in primary syphilis **(Choice A)**, and condylomata **lata** occur during secondary syphilis **(Choice C)**.

The clinical presentation of syphilis occurs in well-defined stages:

- **Primary syphilis** manifests as a painless ulceration with raised, indurated borders. This **chancre** develops at the *Treponema pallidum* inoculation site (most commonly penis or vulva) 1-3 weeks after contact and resolves in 3-6 weeks. The organism commonly disseminates systemically during this stage.
- **Secondary syphilis**, a bacteremic stage that develops 5-10 weeks following chancre resolution, presents with a diffuse macular **rash,** as shown in the exhibit, encompassing the palms and soles. **Condylomata lata**, large gray wartlike growths typically appearing in the genital/perineal region, are another typical manifestation.
- **Latent syphilis** is an asymptomatic period divided into early latent (infection within past year) and late latent (infection >1 year ago).

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The clinical presentation of syphilis occurs in well-defined stages.

Exhibit Display



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another typical manifestation.

- **Latent syphilis** is an asymptomatic period divided into early latent (infection within past year) and late latent (infection >1 year ago).
- **Late (tertiary) syphilis** develops many years after infection in untreated individuals. **Gummas** are characteristic and often begin as painless, indurated granulomatous lesions that progress to white-gray rubbery lesions that may ulcerate. They are most commonly cutaneous but also appear in the subcutaneous tissue, bones, liver, and other organs. Tertiary syphilis can also manifest as cardiovascular involvement with **ascending aortic aneurysms** (with calcification seen on x-ray) and resultant aortic valve **insufficiency** (murmur, high-pitched tambour S2).

Neurosyphilis, which may be asymptomatic or cause subacute meningoencephalitis, tabes dorsalis, or other neurologic sequelae, is a common manifestation of late syphilis but can occur at **any** stage.

(Choice B) Condylomata acuminata are anogenital warts due to human papillomavirus (HPV), the causative agent of cervical cancer. Common strains associated with condylomata acuminata are HPV 6 and 11, which have low oncogenic potential.

(Choice D) Patients with granuloma inguinale, a sexually transmitted disease caused by *Klebsiella granulomatis* (previously *Calymmatobacterium granulomatis*), can have inguinal swelling, ulcers, abscesses, and fistulas. Gram staining of the lesions reveals cells with rod-shaped intracytoplasmic

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Educational objective:
The clinical presentation of tertiary syphilis includes cardiovascular involvement and gummas. Gummas are necrotizing granulomas occurring on the skin, mucosa, subcutaneous tissue, and bones and within other organs. Neurosyphilis can occur at any stage of infection.

Microbiology	Infectious Diseases	Syphilis
Subject	System	Topic

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A 2-month-old girl is brought to the clinic due to perinatal hepatitis B exposure. Her mother is age 22 and immigrated to the United States shortly after giving birth. The pregnancy was complicated by maternal hepatitis B infection. However, the mother received no prenatal or perinatal care and was not diagnosed with chronic hepatitis B until the immigration process. Maternal HBsAg, HBeAg, and anti-HBc are all positive; anti-HBs is negative. The infant has not been evaluated previously and has not received any immunizations or other medications. She is exclusively breast fed and has been growing normally. Vital signs are normal and physical examination is unremarkable. No hepatomegaly or jaundice is seen. The infant's laboratory results will most likely show which of the following?

A. Antibody against HBsAg (anti-HBs)
B. HBeAg
C. Markedly elevated direct bilirubin
D. Markedly elevated liver function tests
E. Neither HBsAg nor anti-HBs

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C. Markedly elevated direct bilirubin
D. Markedly elevated liver function tests
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A. Antibody against HBsAg (anti-HBs) (15%)
B. HBeAg (43%)
C. Markedly elevated direct bilirubin (0%)
D. Markedly elevated liver function tests (7%)
E. Neither HBsAg nor anti-HBs (33%)

Correct
43%
14 mins, 58 secs
10/01/2020

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Perinatal hepatitis B infection	
Risk factors	• Maternal viral load • Maternal HBeAg positive
Clinical findings	• Infants usually immune-tolerant (normal or mildly elevated liver enzymes, no symptoms) • High risk for chronic infection • High viral load & HBeAg positive
Prevention	• Maternal antiviral therapy in some cases • Newborn hepatitis B vaccination & immunoglobulin within 12 hours • Routine immunization • Serology ~3 months after 3rd dose of vaccine

This infant was exposed to hepatitis B virus (HBV) during delivery. Mother-to-child transmission most commonly occurs during **delivery**, but transplacental infection can also occur. Maternal **viral load** and **HBeAg** status are the strongest risk factors for infant infection. Infants born to HBeAg-positive women (as in this case) have a >90% chance of acquiring infection, whereas the chance is less in infants born to

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commonly occurs during **delivery**, but transplacental infection can also occur. Maternal **viral load** and **HBeAg** status are the strongest risk factors for infant infection. Infants born to HBeAg-positive women (as in this case) have a >90% chance of acquiring infection, whereas the chance is less in infants born to HBeAg-negative women.

Viral replication occurs rapidly in infected infants due to immune system immaturity in newborns. As a result, infected infants have high viral loads and HBeAg levels. Despite this high level of replication, infants enter an **immune-tolerant** phase of chronic HBV infection in which they are asymptomatic and have normal or only mildly elevated liver function tests. Over time, chronically infected newborns are at high risk of progression to **cirrhosis** and **hepatocellular carcinoma**. The chance of progression to chronic hepatitis B is 90% without treatment, much higher than the chance of progression in older children and adults. Administration of **hepatitis B vaccine** and **immunoglobulin** as soon as possible after delivery can prevent chronic infection.

(Choice A) Due to their immature immune system, more than 90% of vertically infected infants develop chronic infection (eg, they do not develop anti-HBs and do not clear their HBV infection). Additionally, the infant's mother has chronic disease and lacks anti-HBs, meaning there would be no maternally derived transplacental antibodies. Therefore, anti-HBs would not be expected in this infant.

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infant's mother has chronic disease and lacks anti-HBs, meaning there would be no maternally derived transplacental antibodies. Therefore, anti-HBs would not be expected in this infant.

(Choices C and D) Hepatic injury from hepatitis B is due to the cellular immune response, not by the virus itself. Therefore, infants with HBV infection enter an immune-tolerant phase due to their immature T-cell responses, which limits hepatocyte damage. As a result, laboratory markers of liver injury (eg, liver function tests, direct bilirubinemia) are usually normal or only mildly elevated in HBV-infected neonates.

(Choice E) Perinatally infected infants have rapid appearance of HBsAg within a few days; absence of both HBsAg and anti-HBs at age 2 months would suggest that the infant was not infected. However, this is unlikely as virtually all infants born to HBeAg-positive mothers will be infected perinatally.

Educational objective:

Infants born to HBeAg-positive mothers have a high risk of acquiring perinatal hepatitis B virus (HBV) infection. Infected neonates have high levels of HBV replication and are at high risk for chronic infection, but are usually asymptomatic or have only mildly elevated liver function tests.

References

- Prevention of neonatal hepatitis B virus transmission.
- Natural history of hepatitis B virus infection in children

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A 10-year-old boy is brought to the office due to abrupt onset fever and sore throat that began a day ago. He has had similar illnesses in the past, which were treated with oral antibiotics. The patient has no other medical conditions and has received all recommended vaccinations. Temperature is 38.3 C (101 F). Physical examination shows erythema of the posterior pharyngeal wall and enlarged tonsils, which are covered by white exudate. There are no enlarged cervical lymph nodes. Throat swab specimen is obtained. Which of the following would be most helpful in determining the need for antibiotic treatment in this patient?

A. Gram staining of the swab for gram-positive cocci in chains

B. Serum titer assay for anti-M protein antibodies

C. Serum titer assay for anti-streptolysin O antibodies

D. Swab culture to demonstrate colonies with incomplete hemolysis

E. Swab immunoassay for streptococcal group A antigens

Submit

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A. Gram staining of the swab for gram-positive cocci in chains (21%)

B. Serum titer assay for anti-M protein antibodies (8%)

C. Serum titer assay for anti-streptolysin O antibodies (30%)

D. Swab culture to demonstrate colonies with incomplete hemolysis (4%)

E. Swab immunoassay for streptococcal group A antigens (34%)

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Group A streptococcus (GAS), also called *Streptococcus pyogenes*, is the leading cause of **bacterial pharyngitis** in children and adolescents. Manifestations include **abrupt-onset fever** and **sore throat**; patients may also have nausea, vomiting, and headache. Examination often reveals exudative tonsillopharyngitis and enlarged tonsils. An alternate diagnosis should be suspected in those with manifestations of viral illness (eg, coryza, conjunctivitis, cough, hoarseness, mouth ulcers).

Patients with suspected GAS pharyngitis require **microbiologic testing** prior to initiation of antimicrobials. Throat swab samples are collected in-office and are subsequently evaluated by the following:

- **Rapid antigen detection testing** (RADT) – this immunoassay evaluates for **GAS antigens** and provides rapid, in-office results. However, due to the test's limited sensitivity, patients with negative RADT require throat culture to confirm they do not have the organism.
- **Throat culture** – samples are plated on blood agar and evaluated for **beta-hemolysis** within 48 hours. GAS is beta-hemolytic due to the expression of cytolysins (eg, streptolysin O), which create a broad zone of complete hemolysis (not incomplete hemolysis) around plated colonies **(Choice D)**.

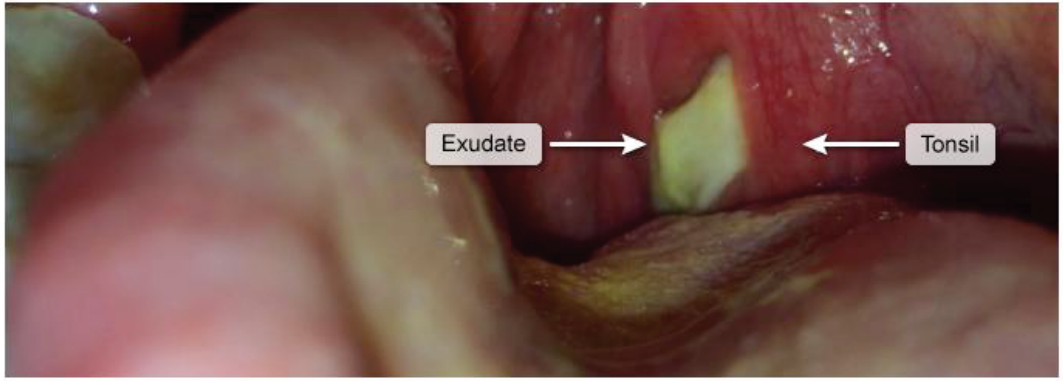
Patients with positive RADT or throat culture require antibiotic therapy (eg, amoxicillin) to prevent complications of GAS (eg, rheumatic fever), limit transmission to others, and reduce duration/severity of

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Exudative pharyngitis



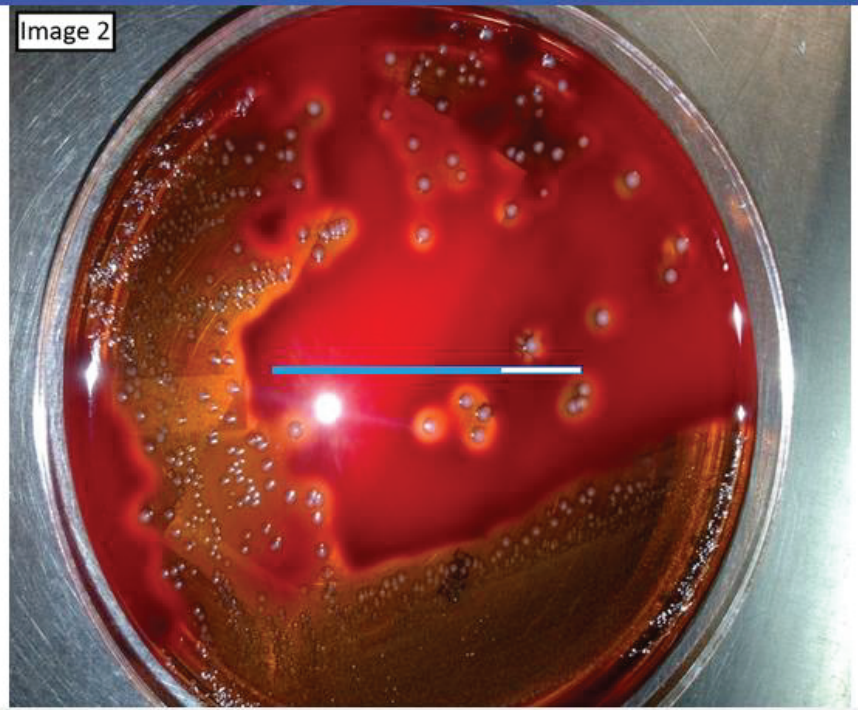
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broad zone of complete hemolysis (not incomplete hemolysis) around plated colonies **(Choice D)**.

Patients with positive RADT or throat culture require antibiotic therapy (eg, amoxicillin) to prevent complications of GAS (eg, rheumatic fever), limit transmission to others, and reduce duration/severity of symptoms.

(Choice A) Gram-stain cannot be used to definitively determine if GAS is present because other oropharyngeal organisms (eg, viridans streptococci) also appear as gram-positive cocci in chains.

(Choice B) Antibodies against M protein, a virulence factor that coats the surface of GAS, provide protective immunity against future infections with a particular GAS strain. However, antibody titers take several weeks to elevate after acute infection; therefore, antibody testing is not used to diagnose acute pharyngitis.

(Choice C) Elevated antibody titers against streptolysin O indicate recent GAS infection and can aid the diagnosis of GAS complications (eg, rheumatic fever, glomerulonephritis). However, antibodies against streptolysin take several weeks to form; therefore, they are not used to diagnose acute pharyngitis.

Educational objective:
Group A streptococcus (GAS) should be suspected in those with acute-onset sore throat, exudative tonsillopharyngitis, and no evidence of viral symptoms (eg, coryza, cough, conjunctivitis). In-office throat

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(Choice A) Gram-stain cannot be used to definitively determine if GAS is present because other oropharyngeal organisms (eg, viridans streptococci) also appear as gram-positive cocci in chains.

(Choice B) Antibodies against M protein, a virulence factor that coats the surface of GAS, provide protective immunity against future infections with a particular GAS strain. However, antibody titers take several weeks to elevate after acute infection; therefore, antibody testing is not used to diagnose acute pharyngitis.

(Choice C) Elevated antibody titers against streptolysin O indicate recent GAS infection and can aid the diagnosis of GAS complications (eg, rheumatic fever, glomerulonephritis). However, antibodies against streptolysin take several weeks to form; therefore, they are not used to diagnose acute pharyngitis.

Educational objective:
Group A streptococcus (GAS) should be suspected in those with acute-onset sore throat, exudative tonsillopharyngitis, and no evidence of viral symptoms (eg, coryza, cough, conjunctivitis). In-office throat swab with rapid antigen detection testing (immunoassay for GAS antigens) can provide on-site microbiologic confirmation, allowing for early initiation of treatment.

Microbiology	Infectious Diseases	Pharyngitis
Subject	System	Topic

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A previously healthy 24-year-old man is hospitalized due to 3 days of fever, chills, myalgia, and severe headache. The symptoms started on the last day of his camping trip in the Appalachian Mountains and have rapidly progressed. Temperature is 38.9 C (102 F), blood pressure is 100/56 mm Hg, and pulse is 120/min. On examination, the patient is lethargic and confused. There is no neck rigidity. The lungs are clear on auscultation and heart sounds are normal. The abdomen is soft and nontender. There is a prominent erythematous maculopapular rash on the distal forearms. No lymphadenopathy is present. The patient should be immediately initiated on a medication that targets which of the following?

A. Bacterial DNA unwinding
B. Bacterial folate metabolism
C. Bacterial protein synthesis
D. Fungal ergosterol synthesis
E. Spirochetal cell wall formation
F. Viral reverse transcription

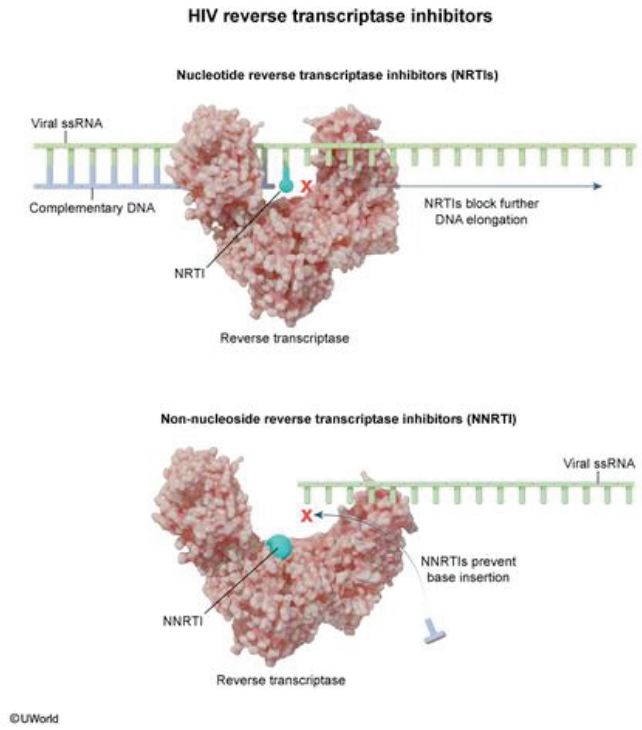
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A 70-year-old man is hospitalized due to abrupt-onset, severe left thigh pain with no preceding trauma. Temperature is 38.9 C (102 F), blood pressure is 90/60 mm Hg, pulse is 120/min, and respirations are 24/min. Left thigh examination shows diffuse swelling with dusky skin discoloration and several bullae filled with hemorrhagic fluid. There is significant tenderness and crepitus on palpation. Gram staining of the bullae fluid reveals numerous gram-positive rods, and subsequent culture grows *Clostridium septicum*. Which of the following is the greatest risk factor for this patient's current condition?

A. Colonic malignancy
B. Hemochromatosis
C. Indwelling vascular catheter
D. Multiple myeloma
E. Recent antibiotic use

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A 70-year-old man is hospitalized due to abrupt-onset, severe left thigh pain with no preceding trauma. Temperature is 38.9 C (102 F), blood pressure is 90/60 mm Hg, pulse is 120/min, and respirations are 24/min. Left thigh examination shows diffuse swelling with dusky skin discoloration and several bullae filled with hemorrhagic fluid. There is significant tenderness and crepitus on palpation. Gram staining of the bullae fluid reveals numerous gram-positive rods, and subsequent culture grows *Clostridium septicum*. Which of the following is the greatest risk factor for this patient's current condition?

- A. Colonic malignancy (19%)
- B. Hemochromatosis (11%)
- C. Indwelling vascular catheter (32%)
- D. Multiple myeloma (10%)
- E. Recent antibiotic use (26%)

Correct

19%
Answered correctly

57 secs
Time Spent

10/13/2020
Last Updated

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Clostridium septicum is a spore-forming, exotoxin-producing, gram-positive bacterium that is a normal commensal of the gastrointestinal tract in humans. Although the organism is largely nonpathogenic, breakdowns in the gastrointestinal mucosa can lead to invasion with subsequent **hematogenous dissemination** to healthy muscle tissue, resulting in **spontaneous gas gangrene** (nontraumatic). Manifestations include **rapid-onset muscle pain**, fever, **hemorrhagic bullae** with dusky surrounding skin, and tissue edema/**crepitus**. Urgent antibiotics and surgery are required, as the infection is often fatal even with early treatment.

Most cases of spontaneous gas gangrene are triggered by an underlying **colonic malignancy**, which creates a portal of entry for the bacteria. Inflammatory bowel disease and immunosuppression are also risk factors. Unlike *C septicum* gas gangrene, *C perfringens* gas gangrene is usually associated with preceding trauma.

(Choice B) Patients with hemochromatosis are at increased risk for fulminant *Vibrio vulnificus* infections (the organism is dependent on free iron for growth). Although *V vulnificus* can cause rapid-onset sepsis and bullous skin lesions, it is a gram-negative bacterium. In addition, most infections occur due to shellfish consumption or wound contamination with seawater.

(Choice C) Indwelling vascular catheters increase the risk for candidemia, which can cause sepsis,

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consumption or wound contamination with seawater.

(Choice C) Indwelling vascular catheters increase the risk for candidemia, which can cause sepsis, abscesses, and pustular skin lesions on an erythematous base.

(Choice D) Multiple myeloma impairs lymphocyte function and reduces the ability of plasma cells to generate normal immunoglobulin, which increases risk of infection. Pneumonia due to *Streptococcus pneumoniae* and *Haemophilus influenzae* and urinary infections due to *Escherichia coli* are most common.

(Choice E) Recent antibiotic use increases the risk of *C difficile* infection, which usually presents with diarrhea, fever, and abdominal pain.

Educational objective:

Clostridium septicum is a spore-forming, exotoxin-producing, gram-positive organism that is the most common cause of spontaneous gas gangrene (eg, rapid-onset pain, hemorrhagic bullae, tissue crepitus). Underlying colonic malignancy is the greatest risk factor for infection.

Microbiology	Infectious Diseases	Clostridial myonecrosis
Subject	System	Topic

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A 26-year-old man is being screened as a potential kidney donor for his mother, who has end-stage renal disease. The patient has no history of diabetes, hypertension, or kidney disease and is up to date with all recommended vaccinations. Physical examination is unremarkable. Blood type and crossmatch testing demonstrate biological compatibility. As part of the evaluation, screening for transmissible diseases is performed and is notable for the following results:

HIV-1 antibody	negative
Hepatitis B core antibody, IgM	negative
Hepatitis B core antibody, IgG	negative
Hepatitis B surface antigen	negative
Hepatitis B surface antibody	positive
Hepatitis C virus	

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HIV-1 antibody	negative
Hepatitis B core antibody, IgM	negative
Hepatitis B core antibody, IgG	negative
Hepatitis B surface antigen	negative
Hepatitis B surface antibody	positive
Hepatitis C virus antibody	negative
Cytomegalovirus antibody, IgM	negative
Cytomegalovirus antibody, IgG	positive

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Cytomegalovirus antibody, IgM	negative
Cytomegalovirus antibody, IgG	positive

Based on these data, the patient most likely has had which of the following conditions in the past?

A. Esophageal ulcer
B. Hepatitis
C. Mononucleosis-like illness
D. Retinitis
E. Vesicular skin rash
F. Viral pneumonia

Submit

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Cytomegalovirus antibody, IgM	negative
Cytomegalovirus antibody, IgG	positive

Based on these data, the patient most likely has had which of the following conditions in the past?

- A. ~~Esophageal ulcer~~ (1%)
- B. ~~Hepatitis~~ (6%)
- ✓ C. Mononucleosis-like illness (81%)
- ✗ D. Retinitis (7%)
- E. ~~Vesicular skin rash~~ (1%)
- F. ~~Viral pneumonia~~ (2%)

Incorrect

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This patient, who is HIV negative, has a positive titer for **cytomegalovirus** (CMV) IgG, suggesting prior CMV infection. CMV is a rare cause of disease in the immunocompetent, with the virus more typically responsible for subclinical infection. When primary CMV infection does result in clinically evident illness, affected individuals appear to have a systemic **mononucleosis-like syndrome** characterized by fever, malaise, myalgia, atypical lymphocytosis, and elevated liver transaminases. In contrast to Epstein-Barr virus mononucleosis (most common), heterophile antibodies are not usually present in patients with CMV mononucleosis (negative Monospot test).

(Choices A and D) Odynophagia (painful swallowing) associated with linear esophageal ulcers due to CMV infection is seen in patients with HIV. Retinitis is one of the most common manifestations of CMV infection in patients with HIV.

(Choice B) Disseminated CMV can cause diarrhea and hepatitis in the immunocompromised. In this patient, the combination of a positive hepatitis B surface antibody with a negative hepatitis B surface antigen and a negative hepatitis B core antibody reflects immunization against hepatitis B, not prior hepatitis B infection.

(Choice E) A vesicular skin rash is seen in association with herpes simplex or herpes zoster virus

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(Choice B) Disseminated CMV can cause diarrhea and hepatitis in the immunocompromised. In this patient, the combination of a positive hepatitis B surface antibody with a negative hepatitis B surface antigen and a negative hepatitis B core antibody reflects immunization against hepatitis B, not prior hepatitis B infection.

(Choice E) A vesicular skin rash is seen in association with herpes simplex or herpes zoster virus infection.

(Choice F) CMV pneumonitis typically occurs after organ transplantation.

Educational objective:
Cytomegalovirus (CMV) is typically associated with subclinical infection in the immunocompetent, with the occasional individual developing a mononucleosis-like syndrome that is heterophile antibody (Monospot) negative. In the immunocompromised, primary or reactivated CMV infection can result in severe retinitis, pneumonia, esophagitis, colitis, or hepatitis.

Microbiology	Infectious Diseases	Cytomegalovirus
Subject	System	Topic

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A 54-year-old man with HIV is part of a large clinical study. He was diagnosed with HIV-1 infection 5 years ago. Blood samples are obtained periodically to perform sequencing analysis of the viral genome. Current testing reveals a large number of isolates with mutation in the *pol* gene compared to the previous analyses. This finding is most closely associated with which of the following?

A. Evasion of humoral immune response
B. Inconsistent use of antiretroviral therapy
C. Ineffective CD8 cytotoxicity
D. Prevention of CD4 cell apoptosis
E. Reduction of viral replication

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A 54-year-old man with HIV is part of a large clinical study. He was diagnosed with HIV-1 infection 5 years ago. Blood samples are obtained periodically to perform sequencing analysis of the viral genome. Current testing reveals a large number of isolates with mutation in the *pol* gene compared to the previous analyses. This finding is most closely associated with which of the following?

A. Evasion of humoral immune response (12%)
✓ B. Inconsistent use of antiretroviral therapy (53%)
C. Ineffective CD8 cytotoxicity (5%)
D. Prevention of CD4 cell apoptosis (6%)
E. Reduction of viral replication (22%)

Correct
53% Answered correctly
01 min, 38 secs Time Spent
01/08/2021 Last Updated

Explanation

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HIV reverse transcriptase does not have a proofreading mechanism. This allows the virus to rapidly accumulate mutations (~1 nucleotide base pair per replication cycle) that may make it resistant to antiretroviral monotherapy. However, the consistent use of **combination antiretroviral therapy**, which contains medications that target multiple steps in the HIV replication cycle, effectively prevents the development of resistant strains.

This patient was found to have a large number of viral isolates with new mutations to the ***pol* gene**, which encodes for the major HIV enzymes protease, reverse transcriptase, and integrase. Most first-line **antiretroviral medications**, including protease inhibitors, reverse transcriptase inhibitors, and integrase strand transfer inhibitors, target these enzymes. The emergence of a new predominant strain with mutation to the *pol* gene suggests that this patient has become resistant to his antiretroviral therapy. Nearly all cases of acquired antiretroviral resistance are due to **inconsistent use** (transmitted resistance can also occur when an individual is inoculated with a resistant strain). This patient will likely need a new antiretroviral regimen and should be encouraged to take it as prescribed.

(Choice A) HIV infection results in the generation of antibodies that can reduce free virus in the circulatory system but cannot eliminate the infection due to viral integration into the host genome. The primary target of neutralizing antibodies against HIV is the surface glycoprotein GP120, which is encoded by the *env* gene, not the *pol* gene.

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system but cannot eliminate the infection due to viral integration into the host genome. The primary target of neutralizing antibodies against HIV is the surface glycoprotein GP120, which is encoded by the *env* gene, not the *pol* gene.

(Choice C) The HIV *nef* gene encodes for a protein that downregulates major histocompatibility complex class I proteins, reducing the ability of cytotoxic T cells to recognize host cells infected with HIV. *Pol* gene mutations are unlikely to directly influence the ability of CD8 cells to respond to the infection.

(Choice D) HIV infection triggers CD4 cell apoptosis through many mechanisms, including chronic immunologic stimulation, activation of the CD4 receptor by envelope glycoproteins (during viral attachment), and increased production of cytotoxic ligands by immune cells. Mutations to the *pol* gene are unlikely to result in a reduction in CD4 apoptosis.

(Choice E) Viral replication rate is generally positively correlated with the mutation rate.

Educational objective:
HIV *pol* gene mutations are responsible for acquired resistance to reverse transcriptase inhibitors, protease inhibitors, and integrase strand transfer inhibitors. Mutations of the *env* gene enable escape from host-neutralizing antibodies.

References

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A previously healthy 24-year-old man is hospitalized due to 3 days of fever, chills, myalgia, and severe headache. The symptoms started on the last day of his camping trip in the Appalachian Mountains and have rapidly progressed. Temperature is 38.9 C (102 F), blood pressure is 100/56 mm Hg, and pulse is 120/min. On examination, the patient is lethargic and confused. There is no neck rigidity. The lungs are clear on auscultation and heart sounds are normal. The abdomen is soft and nontender. There is a prominent erythematous maculopapular rash on the distal forearms. No lymphadenopathy is present. The patient should be immediately initiated on a medication that targets which of the following?

A. Bacterial DNA unwinding
B. Bacterial folate metabolism
C. Bacterial protein synthesis
D. Fungal ergosterol synthesis
E. Spirochetal cell wall formation
F. Viral reverse transcription

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headache. The symptoms started on the last day of his camping trip in the Appalachian Mountains and have rapidly progressed. Temperature is 38.9 C (102 F), blood pressure is 100/56 mm Hg, and pulse is 120/min. On examination, the patient is lethargic and confused. There is no neck rigidity. The lungs are clear on auscultation and heart sounds are normal. The abdomen is soft and nontender. There is a prominent erythematous maculopapular rash on the distal forearms. No lymphadenopathy is present. The patient should be immediately initiated on a medication that targets which of the following?

A. Bacterial DNA unwinding (2%)
B. Bacterial folate metabolism (2%)
✓ C. Bacterial protein synthesis (76%)
D. Fungal ergosterol synthesis (4%)
E. Spirochetal cell wall formation (11%)
F. Viral reverse transcription (2%)

Correct

76%

30 mins, 27 secs

02/02/2021

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This patient developed fever, headache, myalgia, and a maculopapular rash while camping in the Appalachian Mountains, raising strong suspicion for **Rocky Mountain Spotted Fever** (RMSF). The causative pathogen is ***Rickettsia rickettsii***, a weakly gram-negative, obligate intracellular bacterium. Transmission occurs following a **tick bite** from specific tick vectors (eg, American dog tick) present in the eastern and south-central United States and mountainous regions west of the Mississippi River.

R rickettsii moves from the tick salivary glands to the human host after 6-12 hours of attachment. The pathogen enters vascular endothelial cells via endocytosis and subsequently lyses the endosome using specific virulence factors. It then replicates in the cytosol and nucleus of the host cell and spreads rapidly to adjacent cells via filopodia, leading to a lymphohistiocytic **vasculitis**.

Manifestations begin with fever, headache, myalgia, and malaise followed 3-5 days later by a characteristic macular **rash** that becomes petechial over time. The rash typically begins on the ankles or wrists and spreads toward the center of the body (**centripetally**) as well as to the palms and soles. **Thrombocytopenia** frequently occurs as platelets are consumed due to widespread vascular injury. Antibiotic therapy is required to prevent progression and, potentially, death. First-line therapy is **doxycycline**, which **inhibits protein synthesis** by binding the 30s bacterial ribosomal subunit.

(Choice A) Fluoroquinolones prevent DNA gyrase and topoisomerase from unwinding bacterial double-

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(Choice A) Fluoroquinolones prevent DNA gyrase and topoisomerase from unwinding bacterial double-stranded circular DNA. Fluoroquinolones can be used to treat typhoid fever, a *Salmonella* infection that typically occurs in individuals who travel to developing nations. Symptoms include a step-wise fever, salmon-colored rose spots on the trunk, and intestinal bleeding/perforation.

(Choice B) Trimethoprim-sulfamethoxazole inhibits bacterial replication by blocking 2 successive steps in bacterial folate metabolism: Sulfamethoxazole competes with para-aminobenzoic acid in the synthesis of dihydrofolic acid, and trimethoprim inhibits dihydrofolate reductase.

(Choice D) Azole medications inhibit fungal ergosterol synthesis, which disrupts fungal cell membranes. Itraconazole can be used to treat pulmonary histoplasmosis, which usually causes subacute pneumonia with hilar or mediastinal lymphadenopathy.

(Choice E) Penicillin medications inhibit peptidoglycan cross-linking, which disrupts bacterial (spirochetal) cell membranes. Penicillin is the first-line therapy for syphilis, a spirochetal infection that can present with fever and a diffuse, symmetric maculopapular rash that involves the palms and soles (secondary syphilis). However, patients typically have a mild (not high) fever and diffuse lymphadenopathy.

(Choice F) Nucleotide and non-nucleoside reverse transcriptase inhibitors block viral reverse transcription. Although acute retroviral syndrome (early HIV infection) can present with a diffuse

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(Choice E) Penicillin medications inhibit peptidoglycan cross-linking, which disrupts bacterial (spirochetal) cell membranes. Penicillin is the first-line therapy for syphilis, a spirochetal infection that can present with fever and a diffuse, symmetric maculopapular rash that involves the palms and soles (secondary syphilis). However, patients typically have a mild (not high) fever and diffuse lymphadenopathy.

(Choice F) Nucleotide and non-nucleoside reverse transcriptase inhibitors block viral reverse transcription. Although acute retroviral syndrome (early HIV infection) can present with a diffuse maculopapular rash and fever, patients also often have diffuse lymphadenopathy, a sore throat, and painful oral ulcers. In addition, RMSF is more likely in this case given this patient's recent camping trip.

Educational objective:

Rocky mountain spotted fever is a tick-borne illness due to *Rickettsia rickettsii*, a weakly gram-negative, obligate intracellular organism that has an affinity for vascular endothelial cells. Patients usually have nonspecific symptoms (eg, fever, malaise, myalgia) followed by a macular-petechial rash that begins on the ankles and wrists and spreads to the center of the body as well as to the palms and soles. Urgent treatment with doxycycline, an inhibitor of bacterial protein synthesis, is required.

Microbiology Infectious Diseases Rocky mountain spotted fever

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A 14-year-old girl comes to the physician with dark urine and facial puffiness. About 4 weeks before presentation, she had pustular skin lesions that broke down over a few days to form thick scabs in the lower extremities. Microscopic examination of the urine sediment shows red blood cell casts. The organism responsible for this patient's symptoms would most likely demonstrate which of the following?

A. Bile solubility
B. Catalase positivity
C. Growth in hypertonic saline
D. Optochin sensitivity
E. Pyrrolidonyl arylamidase positivity

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A 14-year-old girl comes to the physician with dark urine and facial puffiness. About 4 weeks before presentation, she had pustular skin lesions that broke down over a few days to form thick scabs in the lower extremities. Microscopic examination of the urine sediment shows red blood cell casts. The organism responsible for this patient's symptoms would most likely demonstrate which of the following?

A. Bile solubility (8%)
B. ~~Catalase positivity~~ (14%)
C. ~~Growth in hypertonic saline~~ (4%)
D. Optochin sensitivity (17%)
✓ E. Pyrrolidonyl arylamidase positivity (54%)

Correct

54%
Answered correctly

01 min, 37 secs
Time Spent

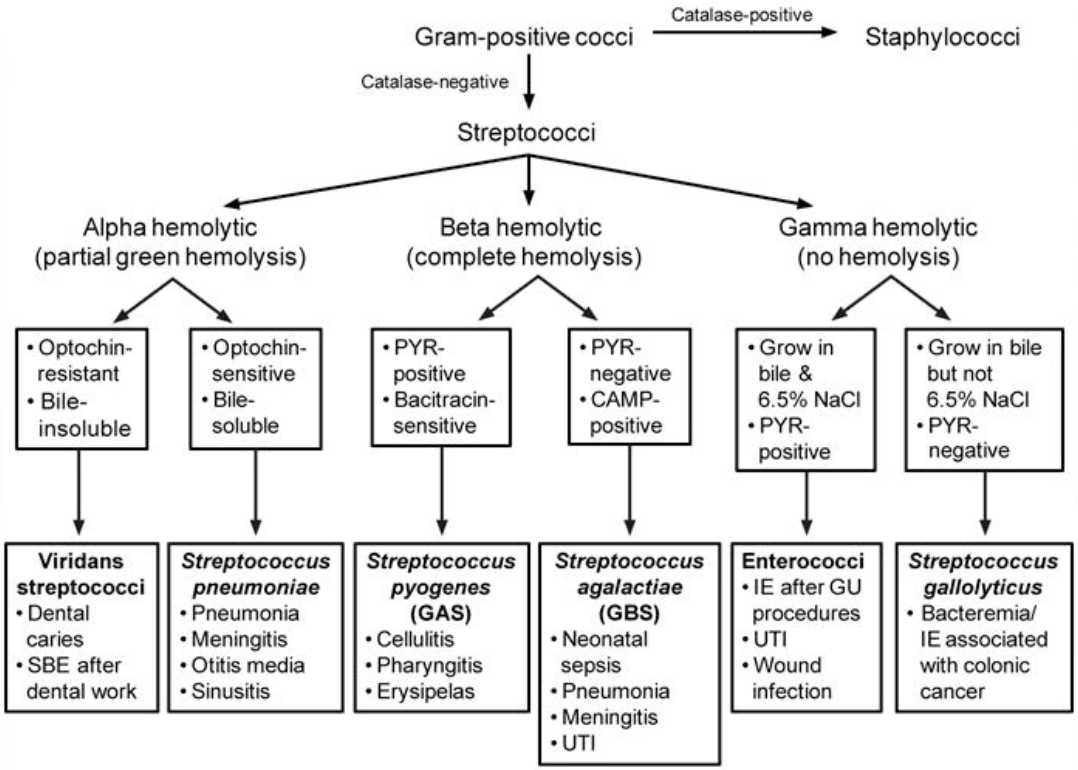
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Last Updated

Explanation

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Microbiological laboratory identification of streptococci



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The patient had **impetigo**, a skin infection caused by *Staphylococcus aureus* and less commonly by *Streptococcus pyogenes* (Group A streptococci [GAS]). Her facial puffiness (likely due to sodium and water retention and possibly proteinuria) and hematuria (likely due to nephritis) suggest post-streptococcal glomerulonephritis. Staphylococcal infection is not complicated by glomerulonephritis, so *S pyogenes* is the most likely causative organism of her symptoms.

Nonsuppurative complications of GAS infections include acute rheumatic fever (ARF) and glomerulonephritis, thought to be due to the formation of different anti-streptococcal antibodies that cross-react with heart tissue or result in immune complex deposition in the kidney. Glomerulonephritis is associated with prior streptococcal pharyngeal or skin infection (eg, cellulitis, impetigo, erysipelas); ARF is associated with prior streptococcal pharyngitis but not skin infection. Previous streptococcal infection is evidenced by elevated streptococcal antibodies (anti-streptolysin, anti-DNaseB, and anti-hyaluronidase).

S pyogenes are catalase-negative, β-hemolytic, gram-positive cocci in chains. *S pyogenes* is unique among β-hemolytic streptococci as it is susceptible to **bacitracin**. Because the bacitracin test is not very specific for *S pyogenes*, it has been replaced in many laboratories by the **pyrrolidonyl arylamidase** (PYR) test; *S pyogenes* is PYR-positive.

(Choices A and D) *Streptococcus pneumoniae* is bile-soluble and optochin-susceptible. These tests are

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(Choices A and D)

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Acute poststreptococcal glomerulonephritis	
Clinical features	• Can be asymptomatic • If symptomatic: ◦ Gross hematuria (tea- or cola-colored urine) ◦ Edema (periorbital, generalized) ◦ Hypertension
Laboratory findings	• Urinalysis: + protein, + blood, ± red blood cell casts • Serum: ◦ ↓ C3 & possible ↓ C4 ◦ ↑ Serum creatinine ◦ ↑ Anti-DNase B & ↑ AHase ◦ ↑ ASO & ↑ anti-NAD (from preceding pharyngitis)

AHase = antihyaluronidase; **anti-DNase B** = antideoxyribonuclease-B; **ASO** = antistreptolysin O; **anti-NAD** = antinicotinamide-adenine dinucleotidase.

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test; *S pyogenes* is PYR-positive.

(Choices A and D) *Streptococcus pneumoniae* is bile-soluble and optochin-susceptible. These tests are used to differentiate *S pneumoniae* from other α-hemolytic streptococci such as those in the viridans group.

(Choice B) Streptococci are catalase-negative, staphylococci are catalase-positive.

(Choice C) Enterococci, not GAS, can grow in broth containing hypertonic (6.5%) saline. Both *S pyogenes* and enterococci are PYR-positive.

Educational objective:

Glomerulonephritis is associated with prior streptococcal pharyngeal or skin infection; acute rheumatic fever is associated with prior streptococcal pharyngitis but not skin infection. Streptococci are catalase-negative, staphylococci are catalase-positive. *Streptococcus pyogenes* (Group A *Streptococcus*) is β-hemolytic, bacitracin-susceptible, and pyrrolidonyl arylamidase-positive. *Streptococcus pneumoniae* is bile-soluble and optochin-susceptible.

Microbiology	Infectious Diseases	Poststreptococcal Glomerulonephritis
Subject	System	Topic

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A 24-year-old pregnant woman comes to the emergency department in active labor at full term. The patient has a history of HIV from injection drug use. She is not adherent with antiretroviral therapy and has had no recent testing of CD4 count or plasma viral load. Physical examination shows regular uterine contractions, ruptured amniotic membranes, and a fully dilated cervix. A decision is made to continue with the vaginal delivery due to advanced labor. Intravenous zidovudine is administered to the patient during the delivery and to the infant immediately after birth. This medication helps decrease the risk of perinatal transmission by inhibiting which of the following components of viral genome replication?

A. Folate-dependent uracil methylation
B. Integration of viral DNA into the host genome
C. Nucleoside phosphorylation
D. Phosphodiester bond formation
E. Proper base pairing and hydrogen bond formation

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A. ~~Folate-dependent uracil methylation~~ (1%)

B. ~~Integration of viral DNA into the host genome~~ (21%)

C. Nucleoside phosphorylation (21%)

D. Phosphodiester bond formation (34%)

E. ~~Proper base pairing and hydrogen bond formation~~ (21%)

Incorrect

34%

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11/22/2020

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A. ~~Folate-dependent uracil methylation~~ (1%)

B. ~~Integration of viral DNA into the host genome~~ (21%)

C. Nucleoside phosphorylation (21%)

D. Phosphodiester bond formation (34%)

E. ~~Proper base pairing and hydrogen bond formation~~ (21%)

Incorrect

34%

02 mins, 04 secs

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HIV is a single-stranded RNA virus that is converted into cDNA by the HIV enzyme **reverse transcriptase**. This enzyme grows DNA by adding nucleotides to the terminal 3′-hydroxyl group using a 3′-5′ **phosphodiester bond**. **Nucleoside reverse transcriptase inhibitors** (NRTIs) such as zidovudine block this step in viral replication. This class of medications is composed of nucleoside/nucleotide analogues that **do not have a 3′-hydroxyl group**. When reverse transcriptase incorporates an NRTI into a growing DNA strand, it results in chain termination because no 3′-hydroxyl group is available to add additional base pairs.

Zidovudine (ZDT) was the first approved HIV medication but is now used primarily to prevent maternal to fetal transmission of HIV during labor and delivery. It is a thymidine analogue that contains an azido group in place of the hydroxyl group usually found at the 3′ end of thymidine.

(Choice A) The enzyme thymidylate synthase catalyzes the conversion of deoxyuridine monophosphate (dUMP) to deoxythymidine monophosphate (dTMP). N5, N10-methylene tetrahydrofolate is the methyl donor in this reaction and is converted to dihydrofolate (DHF) in the process. Tetrahydrofolate is then regenerated from DHF by dihydrofolate reductase. Methotrexate is a chemotherapeutic agent that inhibits DNA synthesis by inhibiting dihydrofolate reductase.

(Choice B) Integration of viral DNA into the host genome is mediated by integrase, an HIV enzyme that is

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inhibited by integrase strand transfer inhibitors (eg, raltegravir).

(Choice C) Inhibition of nucleoside phosphorylation is not an effect of ZDT. In fact, nucleoside reverse transcriptase inhibitors (including ZDT) must be phosphorylated within the host cell to form the functional triphosphate moiety. Non-nucleoside reverse transcriptase inhibitors can bind directly to (and inactivate) reverse transcriptase without being phosphorylated.

(Choice E) In double-stranded DNA, A always pairs with T, and G always pairs with C. These bases bind via hydrogen bonds. Some chemotherapeutic agents, such as the anthracyclines daunorubicin and doxorubicin, intercalate between the bases, causing defective base pairing and splitting of the DNA strands. Transcription and replication failure and mutagenesis ultimately result.

Educational objective:
Zidovudine (ZDT) is a nucleoside reverse transcriptase inhibitor used to prevent maternal to fetal transmission of HIV during labor (when the mother is not virally suppressed). It is a thymidine analogue that does not have the normal 3′-hydroxyl group found on thymidine. Because new nucleotides are added to growing DNA chains only at the 3′-hydroxyl group, the addition of ZDT into DNA results in chain termination.

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A 32-year-old woman comes to the physician for a health maintenance examination. She has been well and has no specific complaints. She eats a well-balanced diet and exercises on a stationary bicycle 3 days a week. She works as a nursing assistant at a local hospital. Review of her records shows that she is due for her annual influenza vaccination. Prior to administration of the vaccine, her skin is disinfected with 70% isopropanol. Which of the following mechanisms is most likely responsible for the antiseptic properties of isopropanol?

A. Coagulation of the cytoplasm
B. Cross-linking of proteins
C. Disruption of cell membranes
D. Halogenation of proteins
E. Production of free radicals

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A 32-year-old woman comes to the physician for a health maintenance examination. She has been well and has no specific complaints. She eats a well-balanced diet and exercises on a stationary bicycle 3 days a week. She works as a nursing assistant at a local hospital. Review of her records shows that she is due for her annual influenza vaccination. Prior to administration of the vaccine, her skin is disinfected with 70% isopropanol. Which of the following mechanisms is most likely responsible for the antiseptic properties of isopropanol?

A. Coagulation of the cytoplasm (2%)
B. Cross-linking of proteins (3%)
✓ C. Disruption of cell membranes (77%)
D. Halogenation of proteins (4%)
E. Production of free radicals (11%)

Correct

77%
Answered correctly

39 secs
Time Spent

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Commonly used clinical disinfectants

Agent	Mechanism	Sporicidal
Alcohols (isopropanol, ethanol)	Disruption of cell membranes Denaturation of proteins	No
Chlorhexidine	Disruption of cell membranes Coagulation of cytoplasm	No
Hydrogen peroxide	Produces destructive free radicals that oxidize cellular components	Yes
Iodine	Halogenation of proteins & nucleic acids	Yes

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Alcohols, including ethanol and isopropanol, are widely used as disinfecting agents in the health care setting. They are commonly used to clean the skin before immunization or venipuncture and to disinfect external surfaces of equipment. They function by disorganizing the lipid structure in membranes, causing them to be leaky, and by denaturing cellular proteins. Alcohols require the presence of water for maximal

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(Choice A) Chlorhexidine works by destabilizing cell membranes and coagulating intracellular constituents. In combination with 70% alcohol, it is the antiseptic of choice for many surgical and percutaneous procedures. Its use is contraindicated in neurologic, otologic, and ophthalmologic procedures due to neurotoxicity.

(Choice B) Formaldehyde and glutaraldehyde function by alkylating and cross-linking DNA and proteins. They are most commonly used for sterilization of hospital instruments that cannot withstand autoclave temperatures.

(Choice D) Iodine causes halogenation of proteins and DNA. Solutions containing iodine are frequently used for antisepsis in surgical and percutaneous procedures. However, they are less effective than chlorhexidine-alcohol and cause more skin irritation and toxicity.

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They are most commonly used for sterilization of hospital instruments that cannot withstand autoclave temperatures.

(Choice D) Iodine causes halogenation of proteins and DNA. Solutions containing iodine are frequently used for antisepsis in surgical and percutaneous procedures. However, they are less effective than chlorhexidine-alcohol and cause more skin irritation and toxicity.

(Choice E) Hydrogen peroxide functions as an oxidant by producing hydroxyl free radicals that attack cellular components. It is excellent at disinfecting inanimate objects but is less effective when used on organic materials. Hydrogen peroxide is often used for skin cleansing and wound debridement due to its effervescent quality.

Educational objective:

Alcohols function by disorganizing the lipid structure in membranes, causing them to be leaky, and by denaturing cellular proteins. They are bactericidal, tuberculocidal, fungicidal, and virucidal, but do not destroy bacterial spores.

References

- Antiseptics and disinfectants: activity, action, and resistance.

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A mother brings her 4-year-old son to see you because he has been experiencing decreased appetite, fever, and right-sided ear discharge for the past 24 hours. His past medical history is significant for three episodes of otitis media over the last year. You prescribe amoxicillin. Adding clavulanic acid to this treatment regimen would serve which of the following purposes?

A. Kill bacteria via a different mechanism of action
B. Decrease amoxicillin cleavage by immune cells
C. Decrease amoxicillin cleavage by bacterial cells
D. Slow liver metabolism of amoxicillin
E. Decrease renal clearance of amoxicillin

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A mother brings her 4-year-old son to see you because he has been experiencing decreased appetite, fever, and right-sided ear discharge for the past 24 hours. His past medical history is significant for three episodes of otitis media over the last year. You prescribe amoxicillin. Adding clavulanic acid to this treatment regimen would serve which of the following purposes?

A. ~~Kill bacteria via a different mechanism of action~~ (4%)
B. ~~Decrease amoxicillin cleavage by immune cells~~ (1%)
C. Decrease amoxicillin cleavage by bacterial cells (86%)
D. Slow liver metabolism of amoxicillin (3%)
E. Decrease renal clearance of amoxicillin (4%)

Correct

86%
Answered correctly

15 secs
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Certain strains of bacteria produce the beta-lactamase enzyme, which hydrolyzes the beta-lactam ring of penicillin family antibiotics rendering them ineffective. To help prevent this effect, beta-lactamase inhibiting compounds have been developed. The beta-lactamase inhibitors include clavulanic acid, sulbactam and tazobactam. Concurrent administration of a beta-lactamase inhibitor with a beta-lactamase susceptible antibiotic allows that antibiotic to retain its efficacy against the offending bacterium. For example, giving clavulanate together with amoxicillin expands amoxicillin's spectrum of activity to include strains of beta-lactamase synthesizing bacteria which would otherwise have been resistant to amoxicillin alone.

(Choice A) Clavulanic acid has negligible intrinsic antibacterial activity.

(Choice B) Immune cells do not produce beta-lactamases.

(Choice D) Clavulanic acid has no effect on the biotransformation of amoxicillin in the liver. Moreover amoxicillin undergoes enterohepatic recirculation and is excreted primarily in unchanged form in the urine.

(Choice E) Probenecid is a compound that decreases the renal clearance of penicillins by inhibiting the tubular organic acid secretion system. This agent has been utilized to prolong the action of penicillin in some settings.

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(Choice E) Probenecid is a compound that decreases the renal clearance of penicillins by inhibiting the tubular organic acid secretion system. This agent has been utilized to prolong the action of penicillin in some settings.

Educational Objective:
Clavulanic acid, sulbactam and tazobactam are beta-lactamase inhibitors. Concurrent administration of clavulanate with amoxicillin expands amoxicillin's spectrum of activity to include strains of β-lactamase synthesizing bacteria that are resistant to amoxicillin alone.

Pharmacology	Infectious Diseases	Penicillin
Subject	System	Topic

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A 23-year-old pregnant woman is found to have chronic viral hepatitis B on liver biopsy. The presence of which of the following serologic markers is most likely to increase the risk of vertical transmission of the virus?

A. HBcAg
B. HBsAg
C. HBeAg
D. Anti- HBcAg IgG
E. Anti- HBeAg IgM
F. Anti-HBsAg IgG

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A 23-year-old pregnant woman is found to have chronic viral hepatitis B on liver biopsy. The presence of which of the following serologic markers is most likely to increase the risk of vertical transmission of the virus?

A. HBcAg (4%)
B. HBsAg (9%)
C. HBeAg (76%)
D. Anti- HBcAg IgG (3%)
E. Anti- HBeAg IgM (3%)
F. Anti-HBsAg IgG (2%)

Correct

76% Answered correctly

21 secs Time Spent

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Vertical transmission of hepatitis B from pregnant females to the unborn child can occur with active hepatitis B infection. Typically, such transmission takes place during the passage of the fetus through the birth canal, but transplacental infection can also occur. This is especially common in those women who developed acute hepatitis B infection in the third trimester.

The presence of HBeAg (a soluble protein that is a marker of viral replication and increased infectivity) in the mother significantly increases the risk of vertical transmission of the virus. Were this woman HBeAg negative, her neonate's risk of infection would be 20%. If she were HBeAg positive, however, her neonate's risk of infection would be 95%. Moreover, should the infant become infected, his chance of progression to chronic hepatitis is 90%. Because of this concern, the newborns of all mothers with active hepatitis B are passively immunized at birth with hepatitis B immune globulin (HBIG), followed by active immunization with recombinant HBV vaccine.

(Choice A) HBcAg is not detectable in serum as it is normally sequestrated within the HBsAg coat.

(Choice B) HBsAg is the first virological marker detected in the serum after inoculation, preceding both the elevation of serum aminotransferases and the onset of clinical symptoms. It remains detectable during the entire symptomatic phase of acute hepatitis B and suggests infectivity. It is not the most ominous marker in

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(Choice B) HBsAg is the first virological marker detected in the serum after inoculation, preceding both the elevation of serum aminotransferases and the onset of clinical symptoms. It remains detectable during the entire symptomatic phase of acute hepatitis B and suggests infectivity. It is not the most ominous marker in the pregnant woman, however.

(Choice D) Anti-HBc appears in the serum shortly after the emergence of HBsAg and remains detectable long after the patient recovers. The IgM fraction signals the acute phase of disease, whereas the IgG fraction signals recovery from the disease. Because IgM anti-HBc is present in the "window period," it is an important tool for diagnosis when HBsAg has been cleared and anti-HBs is not yet detectable. Thus IgM anti-HBc is the most specific marker for diagnosis of acute hepatitis B.

(Choice E) Anti-HBe suggests the cessation of active viral replication and low infectivity.

(Choice F) Anti-HBsAg IgG appears in the serum after either successful HBV vaccination or the clearance of HBsAg and remains detectable for life. It serves as an indicator of noninfectivity and immunity. However, there is a time lag between the disappearance of HBsAg and the appearance of anti-HBs in the serum, which is termed the "window period."

Educational Objective:
Vertical transmission of hepatitis B from pregnant females to the unborn child can occur in women with active hepatitis B infection. The presence of HBeAg (a marker of viral replication and increased infectivity)

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Educational Objective:

Vertical transmission of hepatitis B from pregnant females to the unborn child can occur in women with active hepatitis B infection. The presence of HBeAg (a marker of viral replication and increased infectivity) in the mother greatly increases the risk of vertical transmission of the virus. Because of this concern, the newborns of all mothers with active hepatitis B are passively immunized at birth with hepatitis B immune globulin (HBIG), followed by active immunization with recombinant HBV vaccine.

Microbiology	Infectious Diseases	Hepatitis b
Subject	System	Topic

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A 77-year-old woman is brought to the emergency department due to fever and confusion. The patient has a history of Alzheimer dementia and lives in a nursing home. Temperature is 38.4 C (101.1 F), blood pressure is 104/74 mm Hg, pulse is 110/min, and respirations are 18/min. Suprapubic tenderness is present on physical examination. Urinalysis shows numerous bacteria and leukocytes, and urine culture grows *Pseudomonas aeruginosa*. Further analysis reveals that the isolated organism produces an enzyme that is located on the cytoplasmic surface of the cell membrane and that catalyzes the transfer of acetyl groups to exogenous substances. The bacteria are most likely resistant to which of the following antibiotics?

A. Ceftazidime
B. Ciprofloxacin
C. Gentamicin
D. Imipenem
E. Piperacillin

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a history of Alzheimer dementia and lives in a nursing home. Temperature is 38.4 C (101.1 F), blood pressure is 104/74 mm Hg, pulse is 110/min, and respirations are 18/min. Suprapubic tenderness is present on physical examination. Urinalysis shows numerous bacteria and leukocytes, and urine culture grows *Pseudomonas aeruginosa*. Further analysis reveals that the isolated organism produces an enzyme that is located on the cytoplasmic surface of the cell membrane and that catalyzes the transfer of acetyl groups to exogenous substances. The bacteria are most likely resistant to which of the following antibiotics?

A. Ceftazidime (12%)
B. Ciprofloxacin (13%)
C. Gentamicin (40%)
D. Imipenem (9%)
E. Piperacillin (23%)

Incorrect
Correct answer

40%

02 mins, 04 secs

02/17/2021

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Common antibiotic resistance mechanisms	
Penicillins	• Beta-lactamase, ESBL • Mutated PBP • Mutated porin protein
Vancomycin	• Mutated peptidoglycan cell wall • Impaired influx/increased efflux
Quinolones	• Mutated DNA gyrase • Impaired influx/increased efflux
Aminoglycosides	• Aminoglycoside-modifying enzymes • Mutated ribosomal subunit protein • Mutated porin protein
Tetracyclines	• Impaired influx/increased efflux • Inactivated enzyme
Rifamycins	• Mutated RNA polymerase

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Pseudomonas aeruginosa is a gram-negative, opportunistic pathogen with multiple mechanisms of antibiotic resistance, including beta-lactamases, efflux pumps, and **antibiotic-modifying enzymes**. Antibiotic-modifying enzymes add chemical groups (eg, acetyl, adenyl, phosphate) to a target drug and are the most common mechanisms of **aminoglycoside** (eg, gentamicin) **resistance**. Altered aminoglycosides have a reduced ability to bind to the 16S ribosomal RNA within the 30S ribosomal subunit, leading to increased minimum inhibitory concentrations and reduced bactericidal effects. Most antibiotic-modifying enzymes arise via transfer of plasmids or transposons rather than chromosomal mutations.

(Choices A, D, and E) Cephalosporins (eg, ceftazidime), carbapenems (eg, imipenem), and penicillins (eg, piperacillin) are beta-lactam drugs that exert their effect by interfering with the cell wall. Resistance to cephalosporins and penicillins occurs largely because of the bacterial secretion of beta-lactamase, an enzyme that hydrolyzes the beta-lactam ring and inactivates the antibiotic. Carbapenems are not very susceptible to most beta-lactamases due to additional chemical components surrounding their beta-lactam ring; however, resistance to carbapenems can occur due to carbapenemase, which is primarily seen in *Enterobacter* species.

(Choice B) Fluoroquinolones (eg, ciprofloxacin) block enzymes (DNA gyrase, topoisomerase) responsible for bacterial DNA synthesis. Resistance usually occurs due to genetic mutations that prevent drug binding

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enzyme that hydrolyzes the beta-lactam ring and inactivates the antibiotic. Carbapenems are not very susceptible to most beta-lactamases due to additional chemical components surrounding their beta-lactam ring; however, resistance to carbapenems can occur due to carbapenemase, which is primarily seen in *Enterobacter* species.

(Choice B) Fluoroquinolones (eg, ciprofloxacin) block enzymes (DNA gyrase, topoisomerase) responsible for bacterial DNA synthesis. Resistance usually occurs due to genetic mutations that prevent drug binding to these enzymes or to the increased expression of antibiotic efflux pumps.

Educational objective:

Aminoglycoside (eg, gentamicin) resistance is most commonly due to antibiotic-modifying enzymes. These enzymes add chemical groups to the antibiotic, which diminishes its ability to bind to the 16S ribosomal RNA within the 30s ribosomal subunit.

References

- Mechanisms of antibiotic resistance.

Pharmacology	Infectious Diseases	Aminoglycoside
Subject	System	Topic

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A 43-year-old immigrant from Southern Asia suffers from a cough that has lasted for several months duration. He comes to the clinic today because of recent onset hemoptysis. On further evaluation, he reports a 15-lb weight loss over the past four months. Sputum cultures grow acid-fast bacilli that are susceptible to most antimycobacterial drugs *in vitro*. Isoniazid monotherapy in this patient would most likely result in:

A. Bacteriocidal effect on only extracellular bacilli
B. Decreased transport protein expression on the cell surface
C. β-lactamase induction within bacterial cells
D. Rapid mycobacterial elimination from the body
E. Selective survival of bacterial cells secondary to gene mutation

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A 43-year-old immigrant from Southern Asia suffers from a cough that has lasted for several months duration. He comes to the clinic today because of recent onset hemoptysis. On further evaluation, he reports a 15-lb weight loss over the past four months. Sputum cultures grow acid-fast bacilli that are susceptible to most antimycobacterial drugs *in vitro*. Isoniazid monotherapy in this patient would most likely result in:

A. Bacteriocidal effect on only extracellular bacilli (16%)

B. Decreased transport protein expression on the cell surface (10%)

C. ~~β-lactamase induction within bacterial cells~~ (1%)

D. ~~Rapid mycobacterial elimination from the body~~ (8%)

E. Selective survival of bacterial cells secondary to gene mutation (62%)

Incorrect
Correct answer
E

62%
Answered correctly

02 mins, 33 secs
Time Spent

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This patient most likely has active tuberculosis, which should never be treated with drug monotherapy due to the rapid emergence of antibiotic resistance in *M. tuberculosis*. Isoniazid resistance specifically occurs by two selective gene mutations. The first is a decrease in bacterial expression of the catalase-peroxidase enzyme that is required for isoniazid activation once the drug enters the bacterial cell. The second mechanism of resistance occurs through modification of the protein target binding site for isoniazid. Treatment of active tuberculosis is accomplished by combining multiple antibiotics to avoid selecting for resistant strains. Commonly used drug regimens include isoniazid and rifampin in addition to streptomycin, ethambutol, and/or pyrazinamide.

Isoniazid monotherapy may be used for patients who have a positive PPD and a negative chest x-ray (i.e., no evidence of clinical disease).

(Choice A) For isoniazid monotherapy to result in the selective survival of intracellular bacilli would suggest that isoniazid is unable to penetrate into (or is otherwise degraded by) macrophages that house *M. tuberculosis*. However, this is not the case. Isoniazid can reach therapeutic levels within macrophages, areas of caseous necrosis, and cerebrospinal fluid.

(Choice B) Decreased transport protein expression at the cell surface would interfere with the

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(Choice B) Decreased transport protein expression at the cell surface would interfere with the effectiveness of drugs that require protein-mediated transport into the bacterial cell to reach the intended target (eg, fluoroquinolones, macrolides, aminoglycosides).

(Choice C) β-lactamase induction within bacterial cells would not result from isoniazid exposure because isoniazid is not a beta-lactam antibiotic.

(Choice D) Rapid mycobacterial elimination from the body occurs when a small inoculum is recognized and quickly destroyed by the cell-mediated immune system. This happens in the majority of exposures. By the time tuberculosis has progressed to active, symptomatic disease, large caseous and liquefactive necrotic granulomas have usually formed and a lengthy treatment period with appropriate multidrug therapy is required to eradicate the organism. Antibiotic therapy for tuberculosis lasts a minimum of six months.

Educational Objective:

Active tuberculosis is never treated with drug monotherapy due to the fast emergence of mycobacterial antibiotic resistance from rapid, selective gene mutations. Isoniazid monotherapy may be used for patients who have a positive PPD and a negative chest x-ray (ie, no evidence of clinical disease).

References

- The catalase-peroxidase gene and isoniazid resistance of Mycobacterium tuberculosis.

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A 54-year-old man comes to the hospital due to 4 days of progressive nasal congestion, facial pain, swelling, and fever. The patient has taken over-the-counter decongestants, which provided no relief. He has a history of uncontrolled diabetes mellitus due to dietary and medication noncompliance. The patient's temperature is 38.3 C (101 F). Examination shows right facial swelling and purulent nasal discharge with necrotic destruction of the nasal mucosa and turbinates. The diagnosis of invasive mucormycosis is made, and surgical debridement is performed. He is started on an antifungal agent that binds to ergosterol and alters cell membrane permeability. Considering the adverse effects of this medication, which of the following should be routinely monitored in this patient?

A. Platelet count
B. Serum calcium levels
C. Serum creatine phosphokinase
D. Serum potassium and magnesium levels
E. Thyroid-stimulating hormone

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A. Platelet count (12%)
B. Serum calcium levels (3%)
C. Serum creatine phosphokinase (21%)
D. Serum potassium and magnesium levels (59%)
E. Thyroid-stimulating hormone (3%)

Correct
59%
17 secs
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Mucormycosis should generally be treated with antifungal therapy and surgical debridement. **Amphotericin B** is the initial drug of choice. It binds **ergosterol** in fungal cell membranes to form holes. Resultant changes in membrane permeability lead to cell death. **Renal toxicity** is the most notorious side effect of amphotericin B. The drug causes renal vasoconstriction and a reduction in the glomerular filtration rate. It may also act as a direct toxin on renal epithelial cells, leading to acute tubular necrosis, renal tubular acidosis, and electrolyte disturbances. **Severe hypokalemia and hypomagnesemia** (likely reflecting increased distal tubular membrane permeability) can occur, with most patients requiring supplementation. Renal injury may also lead to decreased erythropoietin production and produce a normochromic normocytic anemia.

Patients with mucormycosis who respond to initial amphotericin therapy may be switched to posaconazole. Liver function test monitoring is recommended in patients taking azoles.

(Choice A) Examples of drugs that can cause isolated thrombocytopenia include heparin, beta-lactam antibiotics, and vancomycin.

(Choice B) Bisphosphonates (used for osteoporosis) affect bone metabolism and can cause hypocalcemia. Foscarnet (used for treating ganciclovir-resistant cytomegalovirus infections) also causes hypocalcemia.

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(Choice A) Examples of drugs that can cause isolated thrombocytopenia include heparin, beta-lactam antibiotics, and vancomycin.

(Choice B) Bisphosphonates (used for osteoporosis) affect bone metabolism and can cause hypocalcemia. Foscarnet (used for treating ganciclovir-resistant cytomegalovirus infections) also causes hypocalcemia.

(Choice C) Daptomycin can induce rhabdomyolysis, leading to elevated creatine phosphokinase.

(Choice E) TSH monitoring is recommended for patients taking amiodarone (used for treating arrhythmias) or lithium (used for treating bipolar disorder).

Educational objective:
Amphotericin B is a polyene antifungal drug notorious for its renal toxicity. Severe hypokalemia and hypomagnesemia are commonly seen during therapy and often require daily supplementation.

Pharmacology	Infectious Diseases	Mucormycosis
Subject	System	Topic

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A 4-year-old boy is brought to the office due to skin lesions on his chin for the past 2 days. Temperature is 36.1 C (97 F). The patient is well-appearing. There are mildly tender perioral papules and pustules, some of which appear to have broken down and are covered with amber-colored crusting. A wound culture is taken, and Gram stain shows gram-positive cocci in chains. Which of the following symptoms would be most likely to develop as a potential complication of this patient's infection?

A. Ascending weakness
B. Facial puffiness and dark urine
C. Fatigue and heart murmur
D. Joint pain and eye redness
E. Unilateral facial drooping

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A. ~~Ascending weakness~~ (0%)
B. Facial puffiness and dark urine (77%)
C. Fatigue and heart murmur (16%)
D. Joint pain and eye redness (5%)
E. Unilateral facial drooping (0%)

Correct

77%
Answered correctly

42 secs
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12/21/2020
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Nonbullous impetigo	
Microbiology	• *Staphylococcus aureus* (most common) • Group A *Streptococcus* (*S pyogenes*)
Clinical features	• Papules & pustules with honey-crusted lesions • May be painful or itchy • Most commonly involves face or extremities in young children
Treatment	• Topical antibiotics (eg, mupirocin) if localized • Oral antibiotics (eg, cephalexin) if extensive
Complications	• Poststreptococcal glomerulonephritis

This child has **impetigo**, a superficial bacterial infection that most commonly develops on the face or extremities in children. Patients usually develop mildly itchy or painful erythematous papules and pustules that later erupt, forming a honey-colored crusting. The most common pathogen is *Staphylococcus aureus* followed by **group A *Streptococcus*** (GAS, *S pyogenes*).

Treatment of localized impetigo is with topical antibiotics (eg, mupirocin), and most patients have no long

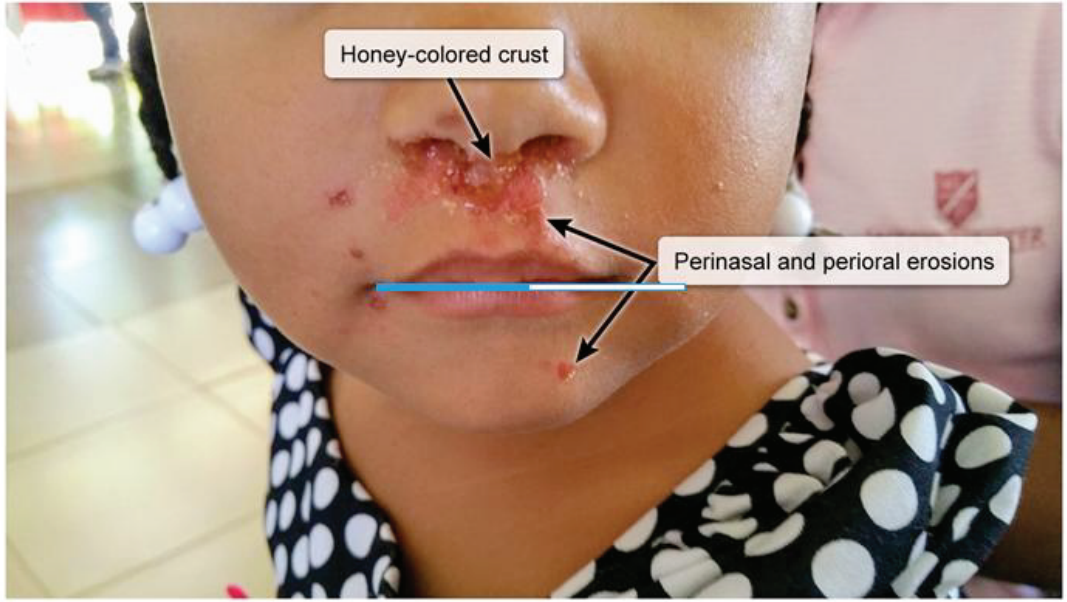
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Impetigo



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Treatment of localized impetigo is with topical antibiotics (eg, mupirocin), and most patients have no long

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Treatment of localized impetigo is with topical antibiotics (eg, mupirocin), and most patients have no long-term sequelae. However, a minority of patients may develop **poststreptococcal glomerulonephritis** (PSGN) several weeks after impetigo caused by GAS (as indicated by this patient's Gram stain showing **gram-positive cocci in chains**). Renal damage is caused by immune complex deposition as well as complement activation, leading to a massive inflammatory response that damages the glomerular basement membrane.

Symptoms of PSGN range from asymptomatic, microscopic hematuria to gross **hematuria** and nephrotic-range **proteinuria**. In addition to tea- or cola-colored urine, patients may develop **periorbital/facial swelling**, generalized edema, and hypertension. Laboratory evaluation typically reveals elevated creatinine and decreased complement C3 level.

(Choice A) Ascending weakness is a classic feature of Guillain-Barre syndrome, which may be preceded by an upper respiratory or gastrointestinal (eg, *Campylobacter jejuni*) infection. GAS disease is not associated with this condition.

(Choice C) Fatigue and a new heart murmur due to carditis can be manifestations of acute rheumatic fever, a potential poststreptococcal sequelae associated with GAS pharyngitis. This disease is not associated with impetigo in developed regions, although this relationship is less clear in some parts of the

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(Choice C) Fatigue and a new heart murmur due to carditis can be manifestations of acute rheumatic fever, a potential poststreptococcal sequelae associated with GAS pharyngitis. This disease is not associated with impetigo in developed regions, although this relationship is less clear in some parts of the developing world.

(Choice D) Eye redness (due to conjunctivitis or anterior uveitis) and joint pain may be seen in reactive arthritis, which typically occurs following a diarrheal (eg, Salmonella) or genitourinary (eg, chlamydial) infection, not impetigo.

(Choice E) Unilateral facial drooping due to a facial nerve palsy (ie, Bell palsy) is often associated with herpes simplex virus infection, not impetigo.

Educational objective:
Poststreptococcal glomerulonephritis is a potential complication of group A streptococcal infection (eg, impetigo, pharyngitis). Symptoms include proteinuria (often associated with periorbital or generalized edema) and hematuria. Acute rheumatic fever is a postinfectious sequelae of streptococcal pharyngitis only, not impetigo.

References

- Impetigo: diagnosis and treatment.

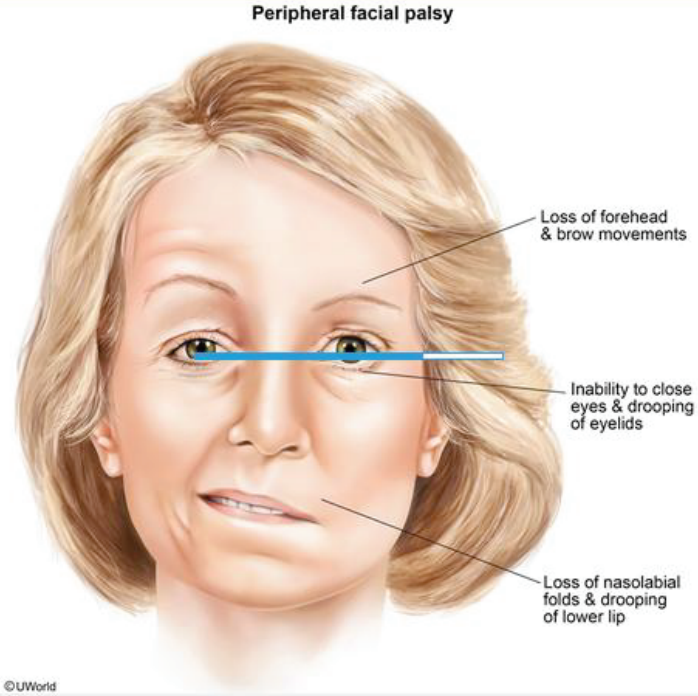
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(Choice C) Fatigue and a new heart murmur due to carditis can be manifestations of acute rheumatic

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A 31-year-old man is brought to the emergency department after a witnessed tonic-clonic seizure. The patient has no known medical conditions. He grew up in a rural part of Guatemala and immigrated to the United States 3 years ago. The patient works as an architect and owns a cat. He has no history of tuberculosis. On examination, the patient is afebrile and has no focal neurologic deficits or meningeal signs. HIV antibody test and interferon-gamma release assay are negative. Chest x-ray is normal. MRI of the brain reveals a 1.5-cm cyst within the left sylvian fissure that has minimal enhancement and no associated edema. Which of the following is the most likely means of acquisition of the infection responsible for this patient's findings?

A. Absorption through the skin of the feet
B. Exposure to infected stool
C. Handling of a cat litter box
D. Inhalation of fungal spores
E. Scratch from a cat
F. Sexual transmission

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United States 3 years ago. The patient works as an architect and owns a cat. He has no history of tuberculosis. On examination, the patient is afebrile and has no focal neurologic deficits or meningeal signs. HIV antibody test and interferon-gamma release assay are negative. Chest x-ray is normal. MRI of the brain reveals a 1.5-cm cyst within the left sylvian fissure that has minimal enhancement and no associated edema. Which of the following is the most likely means of acquisition of the infection responsible for this patient's findings?

- A. Absorption through the skin of the feet (5%)
- B. Exposure to infected stool (39%)
- C. Handling of a cat litter box (32%)
- D. ~~Inhalation of fungal spores~~ (11%)
- E. ~~Scratch from a cat~~ (3%)
- F. ~~Sexual transmission~~ (6%)

Incorrect
Correct answer

39%

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Incorrect
Correct answer

39%

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Neurocysticercosis	
Microbiology	• Ingestion of ***Taenia solium* (pork tapeworm) eggs** excreted in feces of human carriers
Clinical presentation	• Common in **Central & South America**, sub-Saharan Africa, Asia • Prolonged incubation (months to years) • **Seizures**, focal neurologic symptoms, intracranial hypertension (CSF obstruction)
Diagnosis	• CT scan/MRI: **cyst(s)**, **scolex**

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Diagnosis	• CT scan/MRI: **cyst(s), scolex** • **Eosinophilia**, ↑ ESR
Management	• Antiparasitic therapy (albendazole)

CSF = cerebrospinal fluid; **ESR** = erythrocyte sedimentation rate.

This patient who grew up in a rural part of Guatemala and has no underlying immunocompromising conditions had a seizure and is found to have a cystic brain lesion on MRI. This presentation is most consistent with **neurocysticercosis** caused by ***Taenia solium***, the **pork tapeworm**. Although rare in the United States, *T solium* is endemic in **Central and South America** (particularly in rural areas), and neurocysticercosis should be considered in patients from these areas who develop **seizures** or neurologic symptoms.

Consumption of infected uncooked pork, which contains the larval cysts but not the eggs, can lead to tapeworm infestation (taeniasis) but not cysticercosis. In contrast, **ingestion** of eggs from the **stool of tapeworm carriers** can lead to cysticercosis. Once ingested, the eggs hatch into embryos that attach to and penetrate the wall of the small intestine. They subsequently migrate hematogenously to the tissues,

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tapeworm carriers can lead to cysticercosis. Once ingested, the eggs hatch into embryos that attach to and penetrate the wall of the small intestine. They subsequently migrate hematogenously to the tissues, including the brain, where they form **cysticerci**, fluid-filled **larval cysts** surrounding the invaginated scolex (head of tapeworm with hooklets).

(Choice A) *Strongyloides stercoralis* infection can be caused by larvae penetration through the exposed skin of the feet. Manifestations include eosinophilia and gastrointestinal disease (among immunocompetent individuals) or hyperinfection (typically among immunocompromised patients). Brain cysts would be unlikely.

(Choice C) Cat feces may contain *Toxoplasma gondii*. Reactivation of disease in immunocompromised patients, particularly those with AIDS, can cause cerebral toxoplasmosis (multiple ring-enhancing lesions). However, brain infection is exceedingly rare among immunocompetent patients and would be extremely unlikely in this patient who does not have HIV.

(Choice D) Infections caused by endemic dimorphic mycoses, including histoplasmosis and blastomycosis, may be due to spore inhalation. However, neurologic presentations are rare and would be very uncommon in the absence of pulmonary abnormalities.

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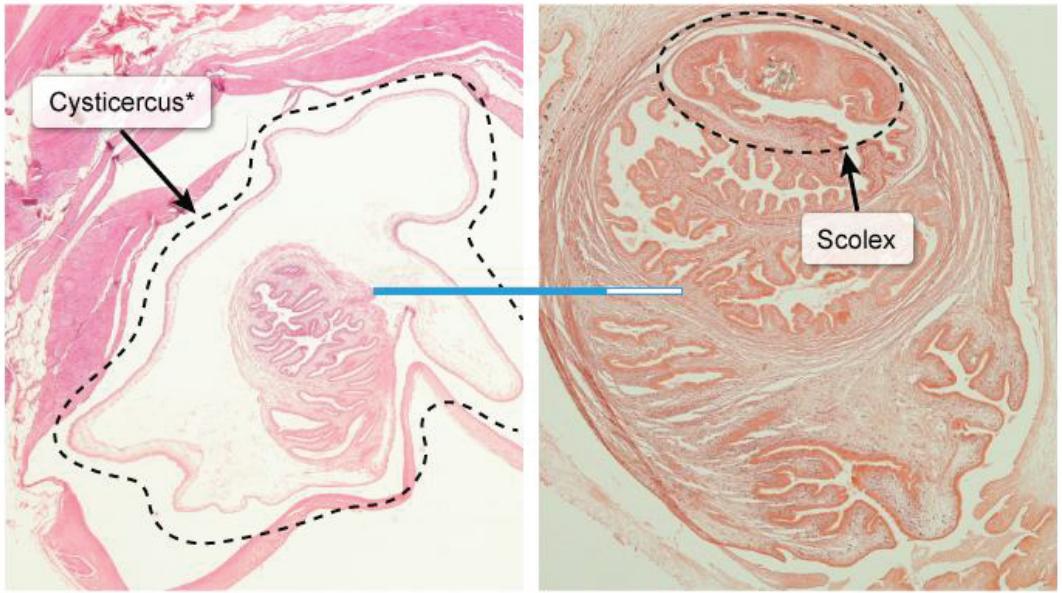
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tapeworm infestation (taeniasis) but not cysticercosis. In contrast, **ingestion** of eggs from the **stool of**

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Cysticercosis



**Taenia solium* larval form

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(Choice E) Cat-scratch disease, caused by *Bartonella henselae*, is most commonly associated with

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blastomycosis, may be due to spore inhalation. However, neurologic presentations are rare and would be very uncommon in the absence of pulmonary abnormalities.

(Choice E) Catscratch disease, caused by *Bartonella henselae,* is most commonly associated with localized skin/soft tissue infection and proximal lymphadenitis.

(Choice F) Herpes encephalitis may present with seizures, but patients are usually febrile, and imaging typically reveals temporal lobe edema or hemorrhage. Syphilis can present with neurologic manifestations, including meningitis, cranial nerve palsies, and tabes dorsalis. However, seizures and a cystic brain lesion in a patient from rural Guatemala are more suggestive of neurocysticercosis.

Educational objective:

Neurocysticercosis is a relatively common cause of seizures in patients from Central and South America and should be considered in patients with suggestive symptoms and imaging (eg, cystic brain lesion) and characteristic epidemiologic risk factors.

References

- Clinical symptoms, diagnosis, and treatment of neurocysticercosis.
- Cysticercosis: an emerging parasitic disease.

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A 1-month-old boy is brought to the emergency department during winter with cough and difficulty breathing. He has had rhinorrhea, cough, and congestion for the past 3 days. Today, the patient began breathing harder and faster with increased cough. Temperature is 37.8 C (100 F) and respirations are 68/min. Oxygen saturation is 91%. The patient is alert and awake and has subcostal and suprasternal retractions. Mucous membranes are moist, and the anterior fontanelle is open and flat. Physical examination reveals diffuse expiratory wheezes and scattered rales. Which of the following pathogens is most likely causing this patient's condition?

A. Adenovirus
B. *Bordetella pertussis*
C. *Mycoplasma pneumoniae*
D. Parainfluenza virus
E. Respiratory syncytial virus
F. *Streptococcus pneumoniae*

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A. ~~Adenovirus~~ (1%)

B. ~~*Bordetella pertussis*~~ (5%)

C. ~~*Mycoplasma pneumoniae*~~ (0%)

D. Parainfluenza virus (6%)

✓ E. Respiratory syncytial virus (85%)

F. ~~*Streptococcus pneumoniae*~~ (1%)

Correct

85%

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11/24/2020

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Bronchiolitis	
Epidemiology	• Age <2 years • RSV most common cause
Clinical presentation	• Antecedent nasal congestion/discharge & cough • Wheezing/crackles & respiratory distress (eg, tachypnea, retractions, nasal flaring) • Apnea in high-risk patients
Treatment	• Supportive care

RSV = respiratory syncytial virus.

This infant with worsening cough and respiratory distress has diffuse wheezing and crackles, findings suggestive of **bronchiolitis**. Bronchiolitis is a lower respiratory tract infection that typically affects children age <2 years, usually during the fall and winter. The most common cause is **respiratory syncytial virus** (RSV).

Initial symptoms include rhinorrhea and congestion, followed by cough, low-grade fever, and increased

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(RSV).

Initial symptoms include rhinorrhea and congestion, followed by cough, low-grade fever, and increased work of breathing. Classic findings include hypoxemia, **tachypnea**, and **retractions** with diffuse **wheezes** and **crackles**. Although illness severity typically peaks at 3-5 days, cough may last several weeks.

In older infants and young children, bronchiolitis is typically a mild, self-limited illness. However, in premature or young (age <2 months) infants, symptoms may be severe (eg, cyanosis, poor perfusion, poor feeding) and lead to apnea and/or respiratory failure.

Diagnosis of bronchiolitis is clinical, and treatment is supportive (eg, supplemental oxygen, nasal suctioning).

(Choices A and D) Adenovirus most commonly causes pharyngitis with conjunctivitis and fever. Parainfluenza virus is the most common cause of croup (laryngotracheobronchitis), which presents with a barky, seal-like cough and inspiratory stridor. Both viruses cause bronchiolitis far less commonly than RSV does.

(Choice B) *Bordetella pertussis* infection in infants classically causes upper respiratory symptoms (eg, rhinorrhea, congestion) with progression to a whooping cough and bouts of coughing and posttussive emesis. In contrast to this patient's examination, the lungs are usually clear to auscultation

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(Choice C) Pneumonia caused by *Mycoplasma pneumoniae* typically presents with fever, cough, and rales and wheezing on examination. However, *M pneumoniae* usually affects children age >5 years and is a rare cause of bronchiolitis.

(Choice F) *Streptococcus pneumoniae* is the most common cause of lobar pneumonia in children and presents with fever and cough. However, examination typically reveals focal rales, not diffuse findings, as seen in this patient.

Educational objective:
Viral bronchiolitis is most commonly caused by respiratory syncytial virus and presents with low-grade fever, cough, and respiratory distress (eg, tachypnea, retractions) in children age <2 years. Examination typically shows diffuse wheezes and/or crackles.

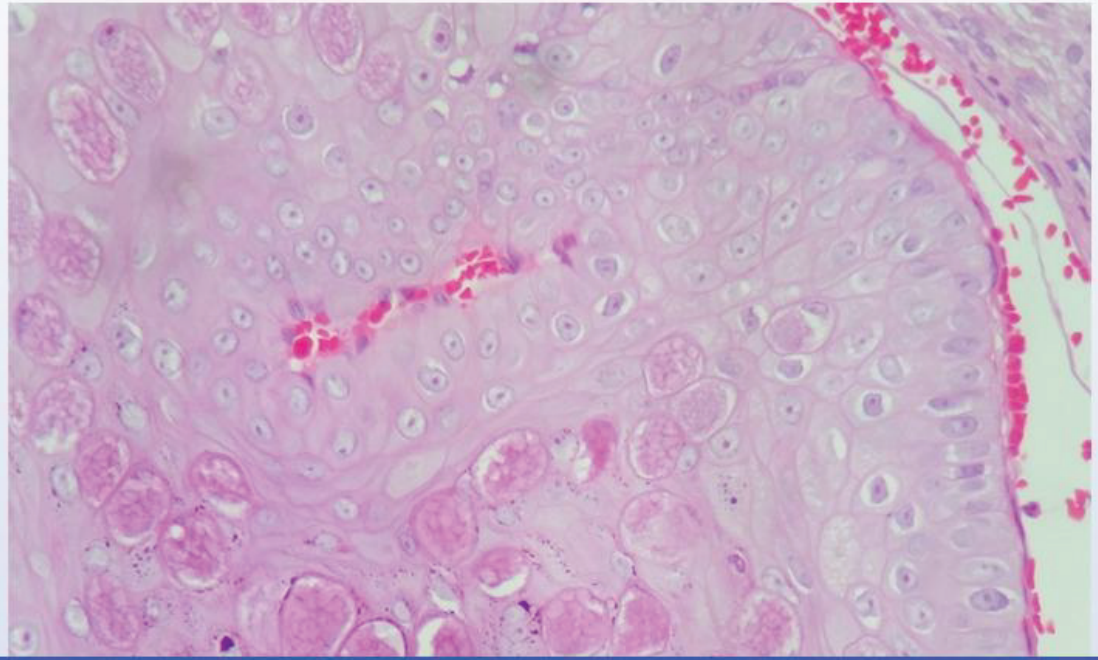
References

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A 43-year-old, HIV-positive woman comes to the office due to lesions on her vulvar and perineal areas for the past 4 weeks. On examination, there are clusters of firm, shiny, round papules that are each 2-6 mm in diameter with central indentation. Microscopic examination of a lesion is shown in the image below:



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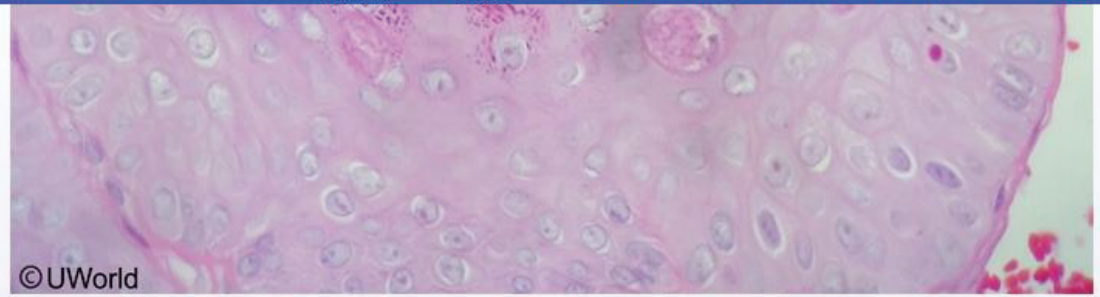
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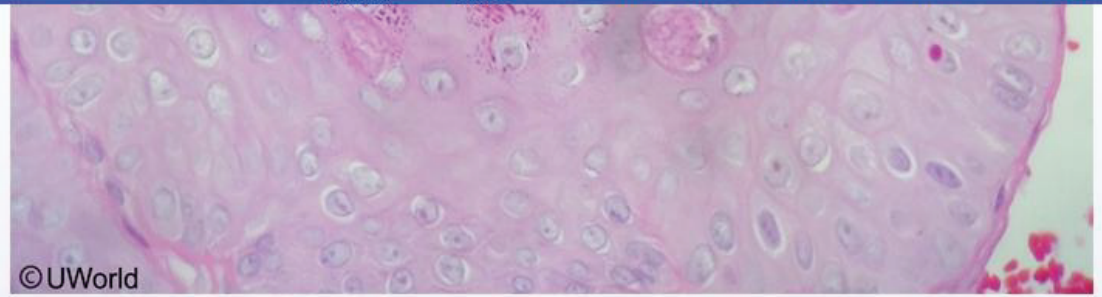
Which of the following is the most likely cause of this patient's presenting condition?

A. Herpes simplex virus
B. Human herpesvirus 8
C. Human papillomavirus
D. Poxvirus
E. *Treponema pallidum*

Submit

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Which of the following is the most likely cause of this patient's presenting condition?

- A. Herpes simplex virus (9%)
- B. Human herpesvirus 8 (4%)
- C. Human papillomavirus (27%)
- D. Poxvirus (55%)
- E. *Treponema pallidum* (1%)

Correct

55%

01 min, 19 secs

02/09/2021

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Molluscum contagiosum	
Pathophysiology	• Cause: poxvirus • Transmission: direct contact, contaminated fomites, autoinoculation • Microscopy: intracytoplasmic eosinophilic inclusion bodies
Clinical features	• Firm, dome-shaped papule with central umbilication • ± Pruritus • Commonly affected areas ◦ Children (most common): trunk, intertriginous areas, face ◦ Adults: groin, genitals, upper thighs ◦ Immunosuppressed: widespread

This patient has molluscum contagiosum (MC), a benign skin condition caused by a **poxvirus**. MC is most common in young children, but older patients who are sexually active, participate in contact sports, or are immunocompromised (eg, HIV) are also at increased risk.

MC classically presents as **firm, shiny, dome-shaped, flesh-colored** papules that often have a **central umbilication**. Lesions are nontender but may be pruritic. Affected areas in adults usually include the

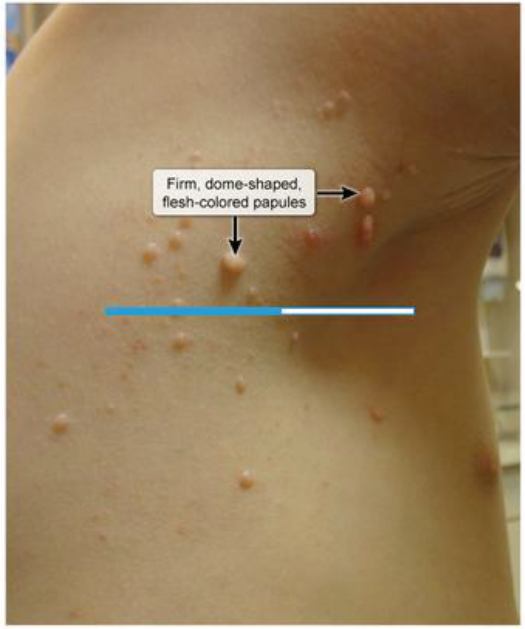
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Exhibit Display

Molluscum contagiosum



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umbilication. Lesions are nontender but may be pruritic. Affected areas in adults usually include the

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umbilication. Lesions are nontender but may be pruritic. Affected areas in adults usually include the lower abdomen, genitalia, and upper thighs because sexual contact is the most common route of transmission. However, autoinoculation can lead to spread on any part of the body (except the palms and soles), and patients who are immunosuppressed are at increased risk for widespread disease.

Microscopy of the lesions shows intracytoplasmic eosinophilic inclusion bodies (molluscum bodies) composed of poxvirus within keratinocytes in the epidermis. Lesions usually self-resolve within 6-12 months but typically last longer in immunocompromised patients.

(Choice A) Genital herpes simplex virus causes acute episodes of painful vesicles and ulcers, which are not present in this patient. In addition, microscopy of herpes shows multinucleated cells.

(Choice B) Human herpesvirus 8 in immunocompromised patients causes Kaposi sarcoma, which typically presents with nontender, discolored (eg, pink, purple, red) papules on the extremities, face, and genitalia. Biopsy shows whorls of spindle cell proliferation and extravasated red blood cells.

(Choice C) Condyloma acuminata (due to human papillomavirus) are typically soft, verrucous anogenital lesions without a central indentation. Microscopy shows papillomatosis and perinuclear cytoplasmic vacuolation (koilocytosis).

(Choice E) Syphilis, caused by *Treponema pallidum*, classically presents with a painless genital ulcer in its

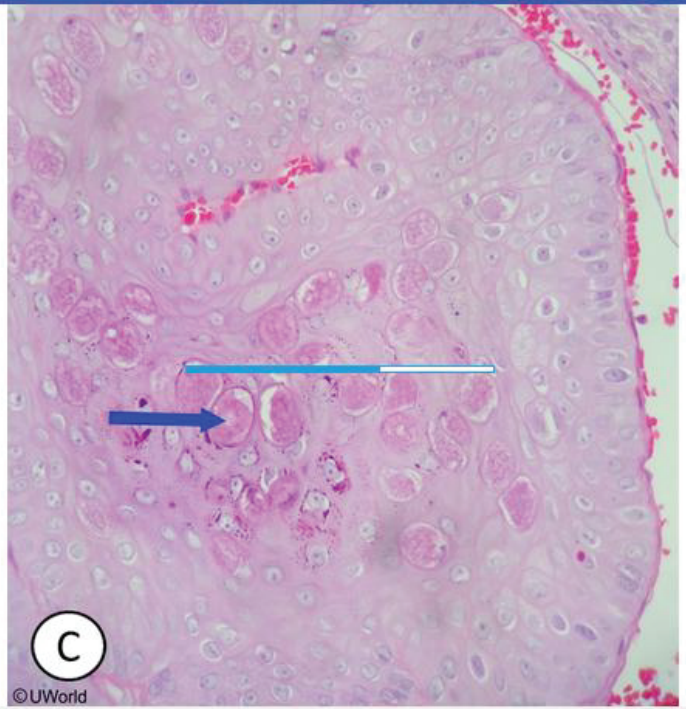
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[Choice E] Syphilis, caused by *Treponema pallidum*, classically presents with a painless genital ulcer in its

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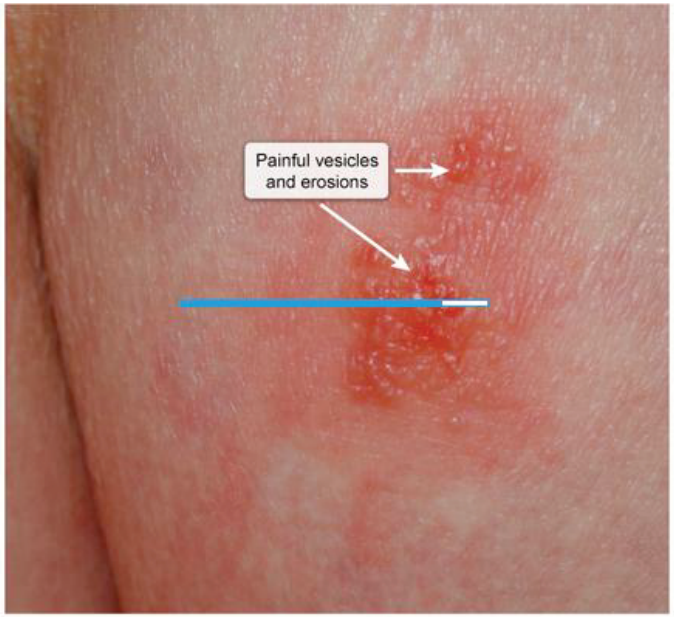
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umbilication. Lesions are nontender but may be pruritic. Affected areas in adults usually include the

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Genital herpes



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[Choice E] Syphilis, caused by *Treponema pallidum*, classically presents with a painless genital ulcer in its

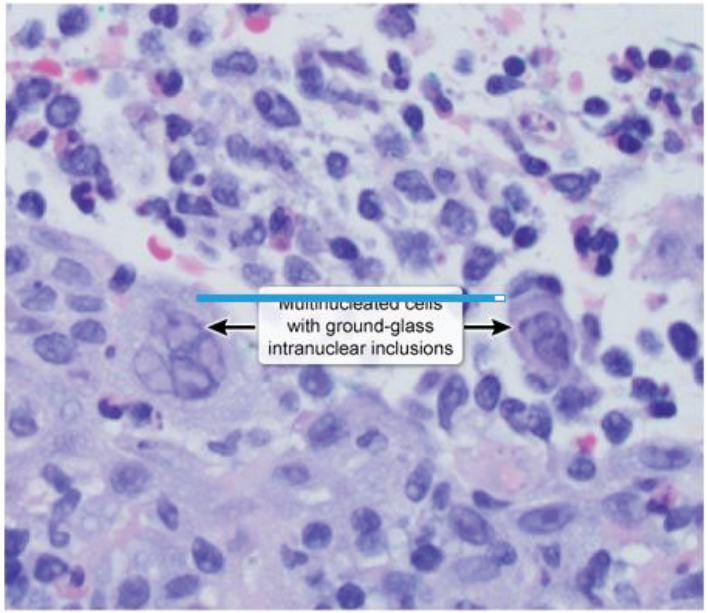
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umbilication. Lesions are nontender but may be pruritic. Affected areas in adults usually include the

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Vulvar herpes simplex (HSV)



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[Choice E] Syphilis, caused by *Treponema pallidum*, classically presents with a painless genital ulcer in its

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umbilication. Lesions are nontender but may be pruritic. Affected areas in adults usually include the

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Kaposi sarcoma



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[Choice E] Syphilis, caused by *Treponema pallidum*, classically presents with a painless genital ulcer in its

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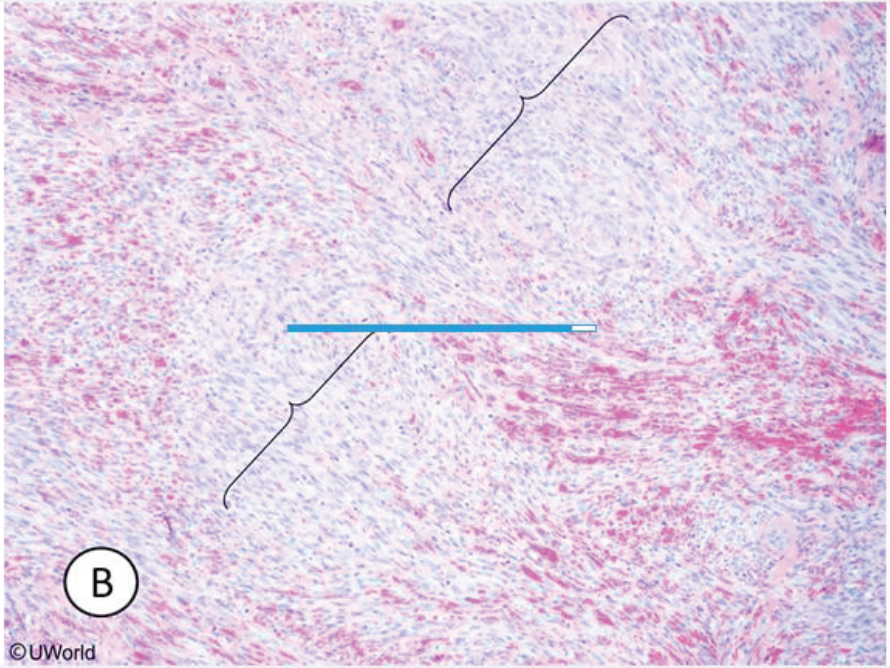
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umbilication. Lesions are nontender but may be pruritic. Affected areas in adults usually include the

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Kaposi sarcoma Kaposi's sarcoma



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[Choice E] Syphilis, caused by *Treponema pallidum*, classically presents with a painless genital ulcer in its

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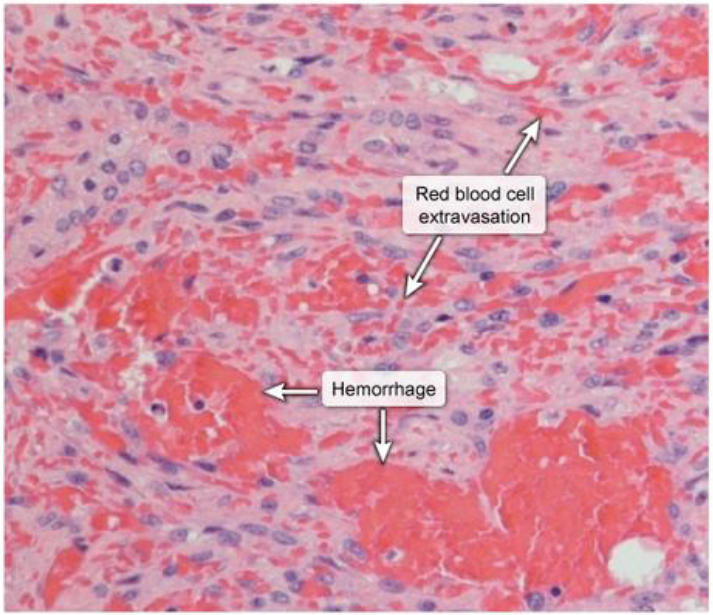
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umbilication. Lesions are nontender but may be pruritic. Affected areas in adults usually include the

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Kaposi sarcoma | Kaposi's sarcoma

Kaposi sarcoma



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umbilication. Lesions are nontender but may be pruritic. Affected areas in adults usually include the

Exhibit Display

Condyloma acuminata



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[Choice E] Syphilis, caused by *Treponema pallidum*, classically presents with a painless genital ulcer in its

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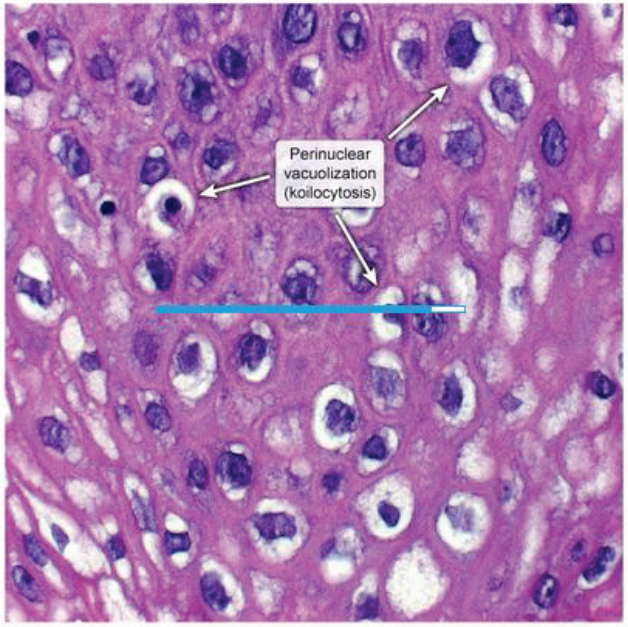
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umbilication. Lesions are nontender but may be pruritic. Affected areas in adults usually include the

Exhibit Display

Condyloma acuminata



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[Choice E] Syphilis, caused by *Treponema pallidum*, classically presents with a painless genital ulcer in its

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genitalia. Biopsy shows whorls of spindle cell proliferation and extravasated red blood cells.

(Choice C) Condyloma acuminata (due to human papillomavirus) are typically soft, verrucous anogenital lesions without a central indentation. Microscopy shows papillomatosis and perinuclear cytoplasmic vacuolation (koilocytosis).

(Choice E) Syphilis, caused by *Treponema pallidum*, classically presents with a painless genital ulcer in its primary stage. Secondary syphilis can cause condyloma lata, which are pale papules and plaque-like genital lesions. Although the diagnosis is normally confirmed through serologic testing, microscopy would show spirochetes on darkfield examination rather than molluscum bodies in keratinocytes.

Educational objective:

Molluscum contagiosum is caused by a poxvirus and presents with small, firm, rounded, papules that often have a central umbilication. Adults who are immunocompromised (eg, HIV) or sexually active are at increased risk. Biopsy shows intracytoplasmic eosinophilic inclusion bodies of poxvirus in keratinocytes.

References

- Molluscum contagiosum: an update and review of new perspectives in etiology, diagnosis, and treatment.

Microbiology Infectious Diseases Molluscum contagiosum

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An infant is evaluated at the office after developing prominent oral thrush, interstitial pneumonia, and severe lymphopenia during the first year of life. The patient was born full-term to a 25-year-old woman who received no prenatal care and is an intravenous drug abuser. She breastfed her son for the first month but then switched to formula feedings. The mother is currently unwilling to undergo any kind of testing. She tells the health care provider, "Just take care of my son." Which of the following prenatal interventions would have most likely prevented this infant's condition?

A. Enzyme inhibitor drug
B. Interferon therapy
C. Killed vaccine
D. Live attenuated vaccine
E. Prenatal vitamins
F. Toxoid vaccine
G. Viral component vaccine

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severe lymphopenia during the first year of life. The patient was born full-term to a 25-year-old woman who received no prenatal care and is an intravenous drug abuser. She breastfed her son for the first month but then switched to formula feedings. The mother is currently unwilling to undergo any kind of testing. She tells the health care provider, "Just take care of my son." Which of the following prenatal interventions would have most likely prevented this infant's condition?

- A. Enzyme inhibitor drug (62%)
- B. Interferon therapy (13%)
- C. Killed vaccine (6%)
- D. Live attenuated vaccine (4%)
- E. Prenatal vitamins (5%)
- F. Toxoid vaccine (3%)
- G. Viral component vaccine (4%)

Correct

62%
Answered correctly

46 secs
Time Spent

02/04/2021
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Oral thrush, interstitial pneumonia, and severe lymphopenia during the first year of life are consistent with mother-to-child **vertical transmission of HIV-1**. The risk of HIV infection occurring in an infant born to an HIV-positive mother who received no prenatal **antiretroviral therapy** (ART) can be as high as 35%. ART during pregnancy reduces the risk of perinatal transmission to 1%-2%. All pregnant women with HIV should take ART, regardless of their CD4 cell count or viral load.

Triple combination therapy is recommended for HIV-positive pregnant women (as it is for all HIV-positive adults) and most commonly has a backbone of 2 nucleoside/nucleotide **reverse transcriptase inhibitors** along with a third drug (protease inhibitor, non-nucleoside reverse transcriptase inhibitor, or integrase inhibitor). Drugs that are associated with a teratogenic risk (eg, efavirenz in first 8 weeks) or for which there is insufficient evidence during pregnancy are to be avoided. ART should be continued as long as women are breastfeeding. Infants generally receive several weeks of prophylaxis (zidovudine).

(Choice B) Interferon-α is used for the treatment of hairy cell leukemia, condyloma acuminata, hepatitis B virus infection, and Kaposi sarcoma.

(Choices C, D, F, and G) There are no vaccines currently available to prevent HIV. Infants whose mothers are HBsAg-positive should receive the hepatitis B vaccine and immunoglobulin within hours of birth to prevent perinatal transmission. There is no effective prevention for mother-to-child transmission of

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(Choice B) Interferon-α is used for the treatment of hairy cell leukemia, condyloma acuminata, hepatitis B virus infection, and Kaposi sarcoma.

(Choices C, D, F, and G) There are no vaccines currently available to prevent HIV. Infants whose mothers are HBsAg-positive should receive the hepatitis B vaccine and immunoglobulin within hours of birth to prevent perinatal transmission. There is no effective prevention for mother-to-child transmission of hepatitis C.

(Choice E) Folic acid in prenatal vitamins (PNVs) can help prevent neural tube defects. Other important PNV components include iron (for hemoglobin synthesis), calcium (for bone growth), and iodine (for thyroid function). PNV intake does not prevent vertical transmission of HIV.

Educational objective:
Antiretroviral therapy during pregnancy reduces the risk of perinatal transmission of HIV to 1%-2% and is recommended for all pregnant women with HIV.

Microbiology	Infectious Diseases	HIV
Subject	System	Topic

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A 54-year-old man comes to the emergency department due to fever, chills, and malaise over the past day. His other medical problems include recently diagnosed Hodgkin disease. Temperature is 39.4 C (103 F), blood pressure is 102/61 mm Hg, and pulse is 114/min. The patient appears ill. Blood cultures grow motile gram-positive rods that produce a very narrow zone of beta hemolysis on blood agar. The bacteria are also found to grow well at refrigerated temperature. Which of the following processes is most important for eliminating these bacteria from the body?

A. Cell-mediated immunity
B. Eosinophil action
C. Immunoglobulin secretion
D. Mast cell activation
E. Terminal complement cascade

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A 54-year-old man comes to the emergency department due to fever, chills, and malaise over the past day. His other medical problems include recently diagnosed Hodgkin disease. Temperature is 39.4 C (103 F), blood pressure is 102/61 mm Hg, and pulse is 114/min. The patient appears ill. Blood cultures grow motile gram-positive rods that produce a very narrow zone of beta hemolysis on blood agar. The bacteria are also found to grow well at refrigerated temperature. Which of the following processes is most important for eliminating these bacteria from the body?

- ✓ A. Cell-mediated immunity (59%)
- B. Eosinophil action (0%)
- C. Immunoglobulin secretion (25%)
- D. Mast cell activation (1%)
- E. Terminal complement cascade (13%)

Correct

59% Answered correctly

56 secs Time Spent

03/12/2021 Last Updated

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Common intracellular pathogens*	
Bacteria	*Chlamydia* *Francisella tularensis* *Legionella* *Listeria monocytogenes* *Mycobacterium* *Neisseria gonorrhoeae* *Nocardia* *Rickettsia* *Salmonella typhi* *Yersinia pestis*
Fungi	*Cryptococcus neoformans* *Histoplasma capsulatum*
Protozoa	*Cryptosporidium parvum* *Leishmania* *Plasmodium*

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Protozoa	*Cryptosporidium parvum* *Leishmania* *Plasmodium* *Toxoplasma gondii* *Trypanosoma*

*Facultative intracellular pathogens are also included.

Listeria monocytogenes is a facultative intracellular, gram-positive rod that produces a **very narrow zone of beta hemolysis** on blood agar (similar to group B *Streptococcus* [*Streptococcus agalactiae*]). *Listeria* is immotile at body temperature but demonstrates **tumbling motility at room temperature**. The pathogen is also distinguished by an ability to multiply at refrigerated temperatures (**cold enrichment**), which is one reason *Listeria* is an important cause of foodborne illness (eg, refrigerated soft cheese, meats, unpasteurized milk).

The elimination of intracellular pathogens is largely reliant on the **cell-mediated immune response** as bacteria within cells are protected from circulating immune factors (eg, antibodies, complement). Cells infected by intracellular bacteria display bacterial protein fragments on their surface, which triggers cell lysis by **cytotoxic T cells**. This releases the organism from the protected intracellular space and exposes it to

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by **cytotoxic T cells**. This releases the organism from the protected intracellular space and exposes it to phagocytosis by macrophages. Although intracellular pathogens can often replicate within inactivated macrophages due to virulence factors that prevent phagolysosome destruction, cytotoxic T-cells release **interferon gamma** to **activate macrophages** leading to the formation of fully mature (acidified) phagolysosomes capable of destroying the bacteria.

As the elimination of *Listeria* is reliant on the cell mediated immune response, patients with **impaired cell-mediated** immunity are at greatest risk for invasive *Listeria* infections (eg, sepsis, meningitis), particularly those at the extremes of age (ie, neonates, elderly) or patients who are immunosuppressed (eg, Hodgkin disease, AIDS) or pregnant.

(Choice B) Eosinophils are a component of the innate immune system and are tasked primarily with the eradication of parasitic infections (eg, helminths). Eosinophils play a minor role in the phagocytosis and destruction of intracellular bacteria.

(Choice C) The humoral immune system secretes immunoglobulins and is largely tasked with eliminating extracellular infections such as *Streptococci* and *Staphylococci*. This system is not able to effectively target intracellular bacteria as immunoglobulins cannot access the intracellular space.

(Choice D) Mast cells contribute to defense against parasites and play an important role in allergic

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intracellular bacteria as immunoglobulins cannot access the intracellular space.

(Choice D) Mast cells contribute to defense against parasites and play an important role in allergic responses, particularly immediate hypersensitivity reactions; they do not confer immunity to intracellular pathogens.

(Choice E) The complement system is part of the innate immune system and aids in the opsonization and destruction of bacteria. The terminal complement components (eg, C5b-C9) create a membrane attack complex to lyse bacteria and are particularly important against *Neisseria* infections.

Educational objective:

Listeria monocytogenes is a facultative, intracellular, gram-positive rod that produces a very narrow zone of beta hemolysis on blood agar, shows tumbling motility at room temperature, and can grow at refrigerated temperatures. Intracellular pathogens such as *Listeria* are largely eliminated by the cell-mediated immune response (eg, T-cells, macrophages, cytokines). Patients with impaired cell-mediated immunity are at risk for invasive *Listeria* infections.

References

- Innate and adaptive immune responses to Listeria monocytogenes: a short overview. Page(s): PMC2042024

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A 2-hour-old girl develops tachypnea and grunting in the newborn nursery. The patient was born via cesarean delivery to a 26-year-old mother, gravida 2 para 2. Respiratory rate is 82/min. The other vital signs are within normal limits. Physical examination shows grunting and subcostal retractions but clear lungs. Blood culture reveals gram-positive rods after 11 hours of incubation. Which of the following pathogens is the most likely cause of this patient's condition?

A. *Clostridium tetani*
B. *Corynebacterium* species
C. *Escherichia coli*
D. *Listeria monocytogenes*
E. *Streptococcus agalactiae*
F. *Streptococcus pneumoniae*

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A 2-hour-old girl develops tachypnea and grunting in the newborn nursery. The patient was born via cesarean delivery to a 26-year-old mother, gravida 2 para 2. Respiratory rate is 82/min. The other vital signs are within normal limits. Physical examination shows grunting and subcostal retractions but clear lungs. Blood culture reveals gram-positive rods after 11 hours of incubation. Which of the following pathogens is the most likely cause of this patient's condition?

- A. *Clostridium tetani* (5%)
- B. *Corynebacterium* species (6%)
- C. *Escherichia coli* (1%)
- ✓ D. *Listeria monocytogenes* (69%)
- E. *Streptococcus agalactiae* (16%)
- F. *Streptococcus pneumoniae* (1%)

Correct

69% Answered correctly

49 secs Time Spent

11/10/2020 Last Updated

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Listeria monocytogenes	
Pathogenesis	• Foodborne outbreaks (replicates in cold temperatures) ◦ Unpasteurized milk ◦ Deli meats • Bacterial invasion of intestinal epithelial cells • Can cross placenta to fetus
Clinical features	• Asymptomatic to febrile gastroenteritis in healthy host • Invasive disease (eg, sepsis, meningitis) in neonates, pregnant women, elderly, immunocompromised
Laboratory findings	• Gram-positive rods on culture (eg, stool, blood, CSF)

CSF = cerebrospinal fluid.

This neonate with **respiratory distress** (eg, tachypnea, grunting, subcostal retractions) and gram-positive rods on blood culture most likely has **neonatal sepsis** due to infection with ***Listeria monocytogenes***. *L monocytogenes* is a facultative intracellular anaerobe that typically causes outbreaks via ingestion of

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This neonate with **respiratory distress** (eg, tachypnea, grunting, subcostal retractions) and gram-positive rods on blood culture most likely has **neonatal sepsis** due to infection with ***Listeria monocytogenes***. *L monocytogenes* is a facultative intracellular anaerobe that typically causes outbreaks via ingestion of contaminated foods (eg, unpasteurized milk, deli meats). The bacteria can replicate at cold temperatures (eg, refrigeration) and can invade the intestinal mucosa once ingested, causing gastroenteritis (eg, fever, vomiting, diarrhea). Most cases in healthy patients are self-limited; however, **pregnant women**, neonates, elderly patients, and **immunocompromised** individuals are at increased risk for invasive disease (eg, bacteremia, meningitis).

Neonatal listeriosis may be acquired during or after delivery or by **transplacental transmission** of the bacteria to the fetus. Infection in late pregnancy can cause fetal distress, premature delivery, or signs of neonatal **sepsis** (eg, respiratory distress, temperature instability) within the first few hours of life, as seen in this patient. Maternal infection in early pregnancy can be more damaging to the fetus, causing granulomatosis infantiseptica (ie, skin lesions, disseminated abscesses/granulomas) and/or fetal demise.

(Choices A and B) *Clostridium tetani* and *Corynebacterium* species (eg, *C diphtheriae*) are also gram-positive rods. However, tetanus usually presents with hypertonicity and spasms, while diphtheria typically causes severe pharyngitis; neonatal infection with either is uncommon in resource-rich countries due to

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granulomatosis infantiseptica (ie, skin lesions, disseminated abscesses/granulomas) and/or fetal demise.

(Choices A and B) *Clostridium tetani* and *Corynebacterium* species (eg, *C diphtheriae*) are also gram-positive rods. However, tetanus usually presents with hypertonicity and spasms, while diphtheria typically causes severe pharyngitis; neonatal infection with either is uncommon in resource-rich countries due to transplacental transfer of neutralizing antibodies from immunized mothers. In addition, neither pathogen causes early-onset neonatal sepsis.

(Choices C and E) *Escherichia coli* and *Streptococcus agalactiae* (group B streptococcus) are the most common causes of neonatal sepsis. However, *E coli* is a gram-negative rod, and *S agalactiae* appears as gram-positive cocci in chains.

(Choice F) *Streptococcus pneumoniae* is a gram-positive diplococcus and a common cause of bacteremia and meningitis in infants age ≥1 month.

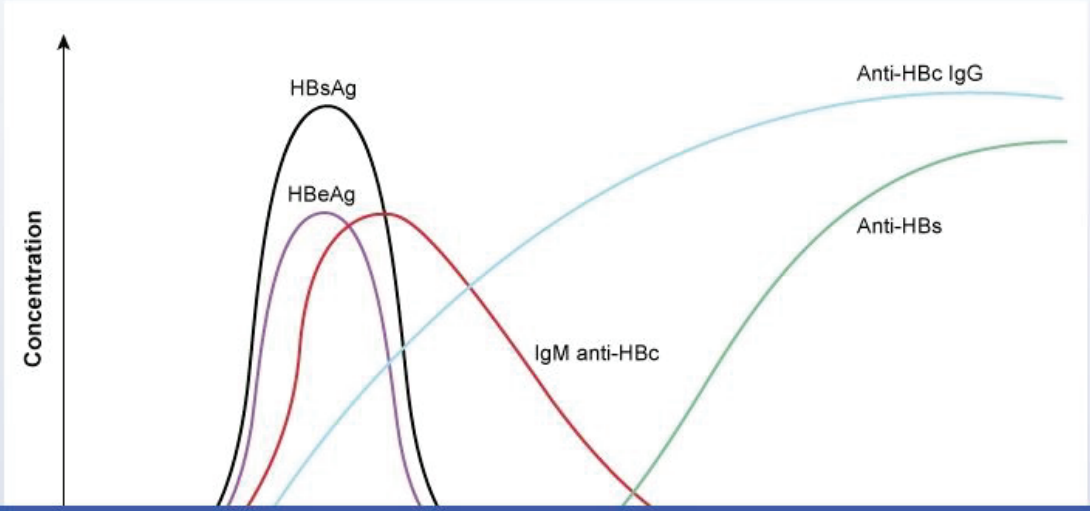
Educational objective:
Listeria monocytogenes is a gram-positive rod associated with outbreaks of gastroenteritis via ingestion of contaminated foods (eg, unpasteurized milk, deli meats). It can cause sepsis in susceptible patients, including neonates, older adults, pregnant women, and immunocompromised individuals.

References

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A 23-year-old man comes to the emergency department due to 7 days of fever and malaise. He has also had nausea and a poor appetite. The patient has no significant medical history but regularly uses injection drugs and has had multiple sexual partners. Temperature is 38 C (100.4 F). On physical examination, there is scleral icterus. A tender, smooth liver edge is palpable 4 cm below the right costal margin. Appropriate therapy is initiated. The following graph illustrates this patient's hepatitis B serologic markers over time.

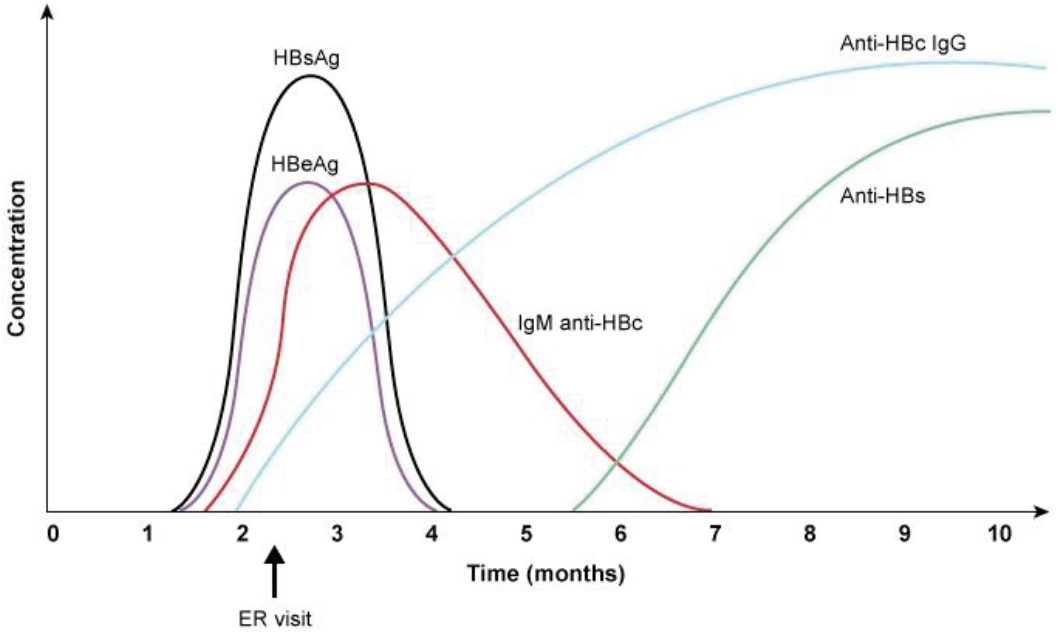


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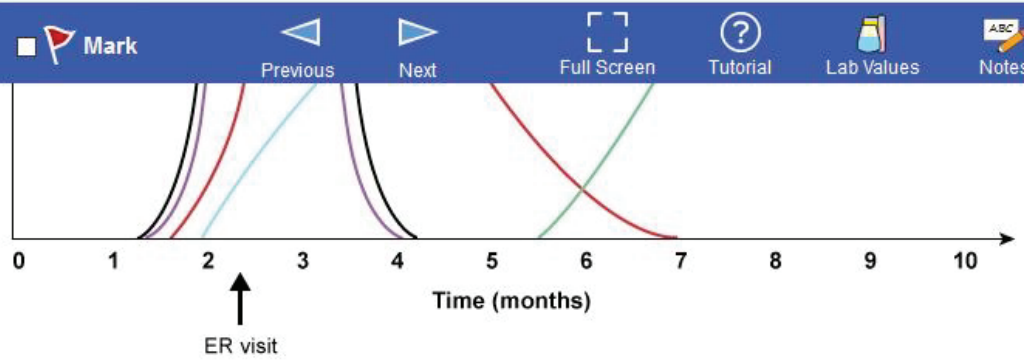
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Which of the following best explains these observed findings?

A. Acute hepatitis B that progressed to chronic hepatitis with high infectivity

B. Acute hepatitis B that progressed to chronic hepatitis with low infectivity

C. Acute exacerbation of pre-existing chronic hepatitis B infection

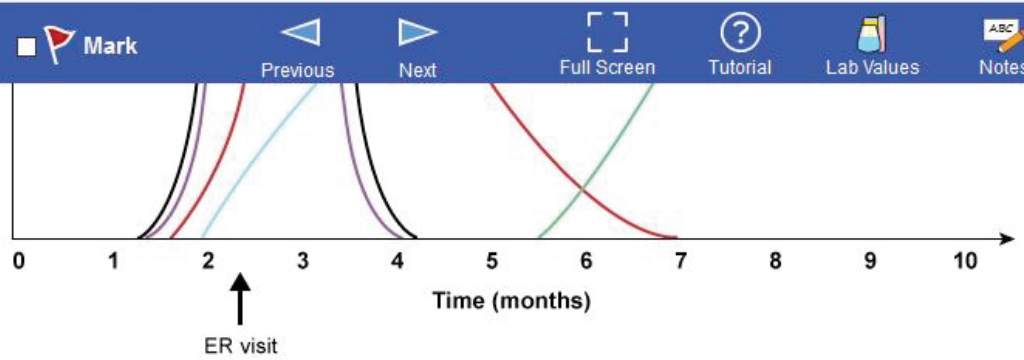
D. Immunity against hepatitis B acquired from vaccination during the hospitalization

E. Recovery from acute hepatitis B infection with immunity against reinfection

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Which of the following best explains these observed findings?

A. ~~Acute hepatitis B that progressed to chronic hepatitis with high infectivity~~ (13%)

B. Acute hepatitis B that progressed to chronic hepatitis with low infectivity (12%)

C. ~~Acute exacerbation of pre-existing chronic hepatitis B infection~~ (3%)

D. ~~Immunity against hepatitis B acquired from vaccination during the hospitalization~~ (3%)

✓ E. Recovery from acute hepatitis B infection with immunity against reinfection (66%)

Correct

66%

47 secs

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Importance of hepatitis B serological markers	
HBsAg	• HBV surface glycoproteins • Detectable during acute infection • Persistence >6 months = **chronic infection**
HBeAg	• HBV polypeptide • Detectable during acute infection • Indicates ↑ **viral replication** & infectivity
Anti-HBc IgM	• First sign of **acute** infection • Present during **window phase** prior to HBsAg & HBeAg
Anti-HBs	• Seen with cleared infection or vaccination • Confers long-term **immunity**
Anti-HBe	• Develops in cleared infection & later in chronic infection • Indicates ↓ **viral replication** & infectivity
Anti-HBc IgG	• Present in both acute & chronic infection

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Anti-HBe	• Indicates ↓ **viral replication** & infectivity
Anti-HBc IgG	• Present in both acute & chronic infection • **Not present** after vaccination

Serologic evidence of **hepatitis B virus** (HBV) exposure is present in ~2 billion people worldwide. Perinatal transmission is most common in high-incidence areas (eg, sub-Saharan Africa). In low-prevalence countries such as the United States, Western Europe, and Canada, most cases arise due to unsafe sexual practices or **injection drug use**.

Serological markers for HBV can be used to distinguish between acute infection, chronic infection, and a protective vaccination response. **Acute** HBV infection is marked by the proliferation of the virus in hepatocytes with the release of viral antigens (**HBsAg**, **HBeAg**) and **HBV DNA** into the bloodstream and the generation of **IgM against HB core antigen**. Many patients with acute infection will have subclinical, anicteric disease, but approximately 30% develop several weeks or months of jaundice, fatigue, hepatomegaly, and elevated transaminases.

Most adults with HBV clear the virus and generate protective immunity against future infection. This is reflected serologically by the following progression:

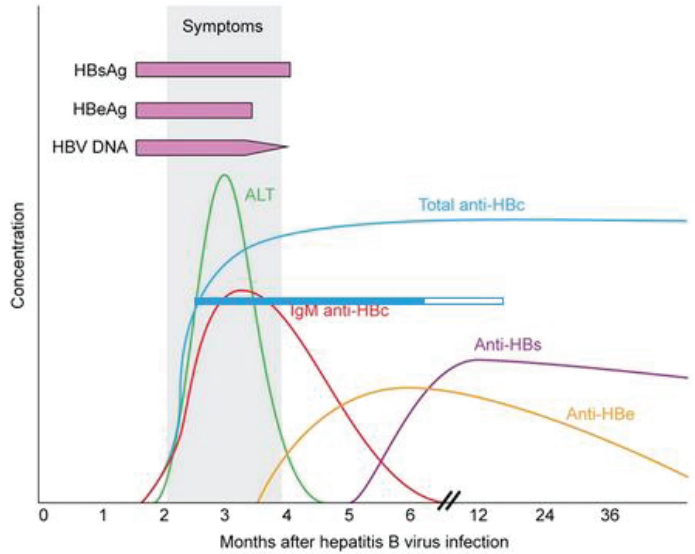
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Anti-HBe

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Acute hepatitis B infection



ALT = alanine aminotransferase; **anti-HBc** = hepatitis B core antibody; **anti-HBe** = hepatitis B e antibody; **anti-HBs** = hepatitis B surface antibody; **HBeAg** = hepatitis B e antigen; **HBsAg** = hepatitis B surface antigen; **HBV** = hepatitis B virus.

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1. **Anti-HBe** antibodies develop 3-6 months after initial infection and are associated with the elimination of HBeAg. This correlates with reduced viral replication and infectivity.
2. HBsAg is eliminated around the time that HBeAg becomes undetectable.
3. **Anti-HBsAg** antibodies form several weeks/months later and provide **protective immunity** against future infection.

(Choices A and B) Patients with chronic hepatitis B have elevated HBsAg >6 months after initial infection. Chronic hepatitis B with high infectivity is represented by persistent elevation of HBsAg, HBeAg, and HBV DNA with no anti-HBe. Transition from high infectivity to low infectivity usually occurs years later and is marked by anti-HBe, the elimination of HBeAg, and the continued production of HBsAg.

(Choice C) Patients with an exacerbation of chronic hepatitis B have an abrupt increase in liver enzymes and increased levels of HBV DNA. Exacerbations are often asymptomatic, but some individuals develop symptoms of acute hepatitis.

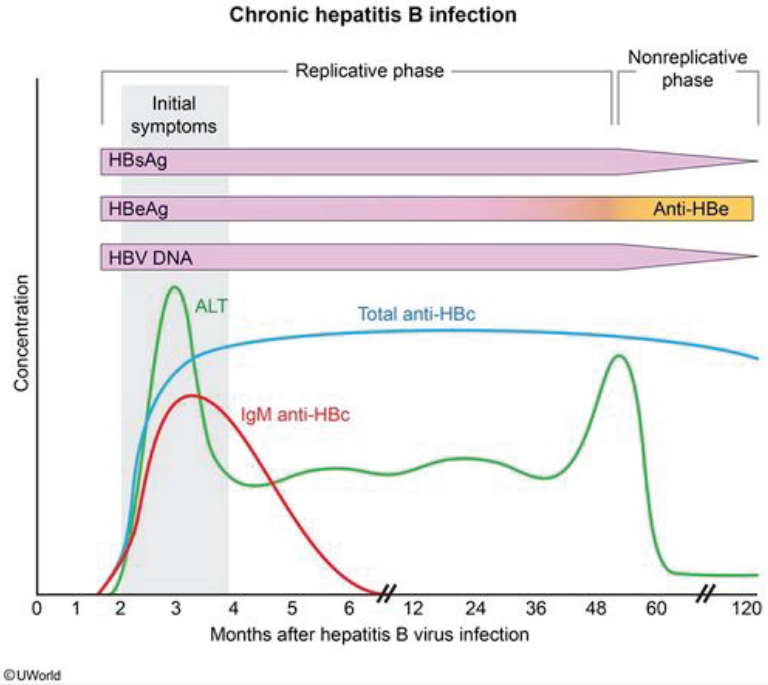
(Choice D) Vaccination against hepatitis B would be identified by the presence of anti-HBs with no anti-HBc, anti-HBe, or viral antigens.

Educational objective:

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Educational objective:

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(Choices A and B) Patients with chronic hepatitis B have elevated HBsAg >6 months after initial infection. Chronic hepatitis B with high infectivity is represented by persistent elevation of HBsAg, HBeAg, and HBV DNA with no anti-HBe. Transition from high infectivity to low infectivity usually occurs years later and is marked by anti-HBe, the elimination of HBeAg, and the continued production of HBsAg.

(Choice C) Patients with an exacerbation of chronic hepatitis B have an abrupt increase in liver enzymes and increased levels of HBV DNA. Exacerbations are often asymptomatic, but some individuals develop symptoms of acute hepatitis.

(Choice D) Vaccination against hepatitis B would be identified by the presence of anti-HBs with no anti-HBc, anti-HBe, or viral antigens.

Educational objective:

The presence of anti-HBc and anti-HBs antibodies in the serum without detectable viral antigens indicates recovery from acute hepatitis B infection. In contrast, patients vaccinated against hepatitis B will have anti-HBs antibodies without detectable levels of anti-HBc. Chronic hepatitis B is indicated by persistent levels of HBsAg and HBV DNA in the serum.

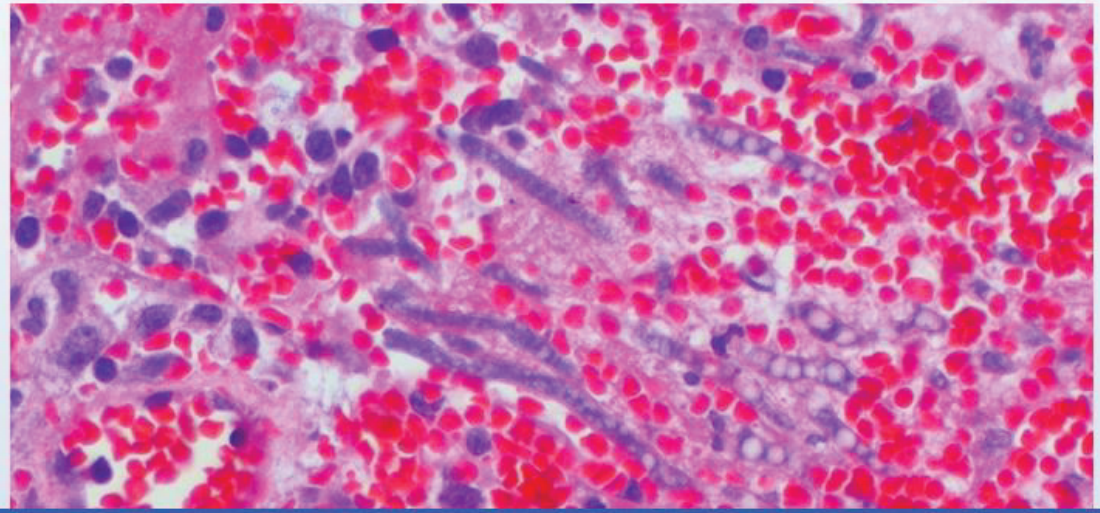
References

- The laboratory diagnosis of hepatitis B virus.

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A 47-year-old man initially comes to his primary care physician with persistent fever, night sweats, and fatigue. Thorough evaluation yields a diagnosis of chronic myeloid leukemia. While undergoing treatment for his malignancy, the patient comes to the oncologist complaining of headaches, scant nasal discharge, and a problem with his left eye. Physical examination reveals tenderness over the paranasal sinuses in addition to left-sided orbital swelling and cellulitis. Mild proptosis and ptosis of the left eye are also present. Biopsy of his sinus mucosa is shown below.



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Which of the following is the most likely cause of this patient's condition?

A. *Aspergillus fumigatus*
B. *Blastomyces dermatitidis*
C. *Candida albicans*
D. *Coccidioides immitis*
E. *Cryptococcus neoformans*
F. *Histoplasma capsulatum*
G. *Malassezia furfur*
H. *Microsporum canis*
I. *Rhizopus species*
J. *Sporothrix schenckii*

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Which of the following is the most likely cause of this patient's condition?

- ✓ A. *Aspergillus fumigatus* (35%)
- B. ~~*Blastomyces dermatitidis*~~ (1%)
- C. ~~*Candida albicans*~~ (4%)
- D. ~~*Coccidioides immitis*~~ (1%)
- E. ~~*Cryptococcus neoformans*~~ (3%)
- F. ~~*Histoplasma capsulatum*~~ (1%)
- G. ~~*Malassezia furfur*~~ (3%)
- H. ~~*Microsporum canis*~~ (0%)
- I. ~~*Rhizopus species*~~ (45%)
- J. ~~*Sporothrix schenckii*~~ (0%)

Correct

35%
Answered correctly

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Time Spent

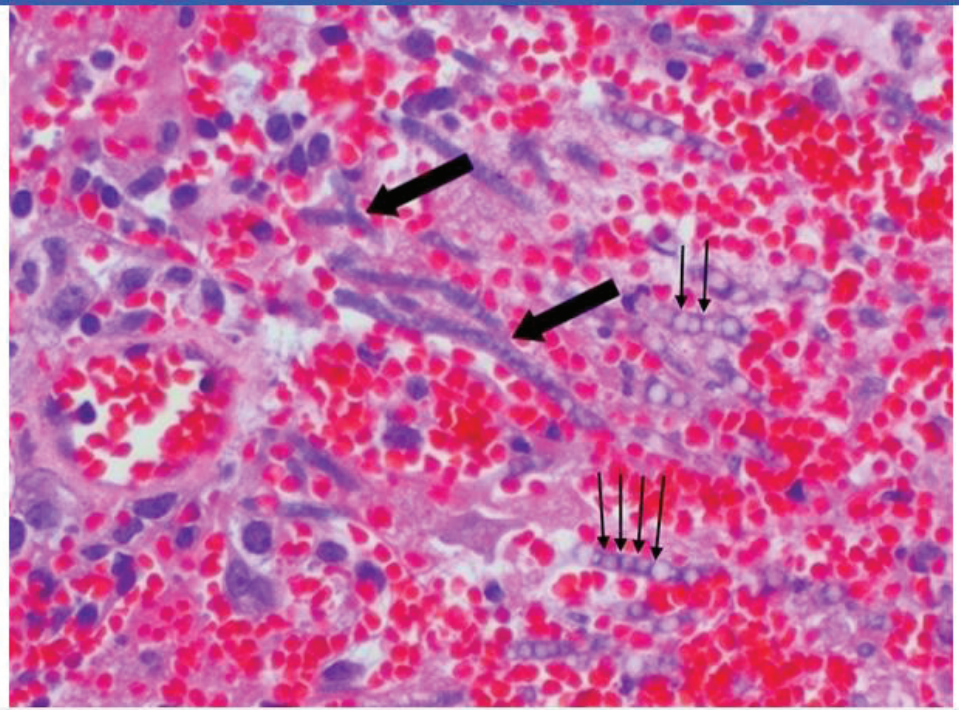
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This patient's symptoms are consistent with fungal rhinosinusitis. The biopsy image shows fungal hyphae branching at acute angles (thick arrows) with septations (thin arrows), which is characteristic of *Aspergillus fumigatus*. This fungus is widely distributed in the environment and commonly grows on decaying vegetables. It is monomorphic, existing only in mold form (ie, multicellular hyphae).

Aspergillus causes the following conditions:

1. **Invasive aspergillosis** develops in **immunosuppressed patients**. The prolonged neutropenia associated with leukemia and lymphoma treatment is a strong risk factor for invasive aspergillosis. It most commonly affects the lung, causing the formation of lung granulomas with development of fever, pleuritic chest pain, and hemoptysis. *Aspergillus* has a predilection for blood vessels and can spread hematogenously, causing infection and infarcts involving the skin, paranasal sinuses, kidneys, endocardium, and brain. Diagnosis is made by light microscopy of tissue specimens, which shows V-shaped, narrow, septate hyphae invading the tissue. Amphotericin B is used to treat invasive aspergillosis.
2. **Aspergillomas** are **fungus balls** caused by *Aspergillus* that grow in old lung cavities (eg, produced by tuberculosis or bronchiectasis). Aspergillomas are limited to the preexisting cavity; invasion of the surrounding lung tissue is rare in immunocompetent patients. They are often surgically removed.

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2. **Aspergillomas** are **fungus balls** caused by *Aspergillus* that grow in old lung cavities (eg, produced by tuberculosis or bronchiectasis). Aspergillomas are limited to the preexisting cavity; invasion of the surrounding lung tissue is rare in immunocompetent patients. They are often surgically removed.
3. **Allergic bronchopulmonary aspergillosis** occurs in patients with asthma and presents with wheezing and have migratory pulmonary infiltrates. Increased serum IgE and increased titers of antibodies against *Aspergillus* are characteristic. Treatment is with corticosteroids.

(Choices B, D and F) *Blastomyces*, *Histoplasma*, and *Coccidioides* are dimorphic fungi. They grow as molds in nature but exist in the human body in yeast form (*Coccidioides* exists in endospore form at body temperature). As a result, hyphae would not be seen in biopsy specimens.

(Choice C) *Candida albicans* is a component of normal human mucous membrane flora. On light microscopy, it appears as an oval budding yeast with pseudohyphae (ie, not true hyphae but rather elongated yeast cells).

(Choice E) *Cryptococcus neoformans* causes meningitis and lung infections in patients with AIDS. It is an oval budding yeast with a thick capsule. India ink stain of the cerebrospinal fluid shows a wide clear zone around the cell corresponding to the unstained capsule.

(Choice I) ***Rhizopus*** and *Mucor* form broad, ribbon-shaped, **non-septate** hyphae that branch at **wide**

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around the cell corresponding to the unstained capsule.

(Choice I) ***Rhizopus*** and *Mucor* form broad, ribbon-shaped, **non-septate** hyphae that branch at **wide angles**. They cause mucormycosis, which typically presents as a paranasal infection in immunocompromised patients or those with diabetes mellitus. However, *Aspergillus* can also cause rhinosinusitis identical in presentation to mucormycosis. The presence of narrow hyphae with septations makes invasive aspergillosis a better diagnosis.

Educational objective:

Immunosuppressed patients are at risk for *Aspergillus fumigatus* infection. This fungus produces thin, septate hyphae with acute V-shaped branching. It causes invasive aspergillosis, aspergillomas, and allergic pulmonary aspergillosis.

References

- Fungal infections in leukemia patients: how do we prevent and treat them?
- Fungal rhinosinusitis: a categorization and definitional schema addressing current controversies.

Microbiology	Infectious Diseases	Aspergillosis
Subject	System	Topic

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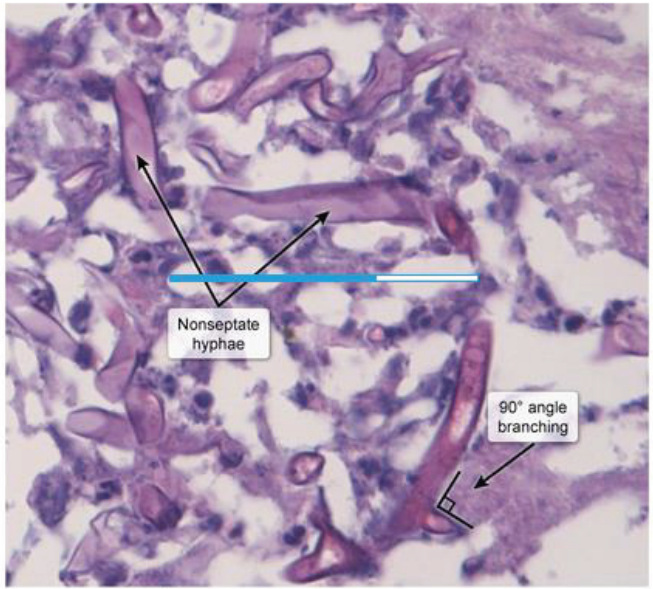
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Mucormycosis Abdominal Mucormycosis

Mucormycosis*



*Frequently due to *Rhizopus* or *Mucor*

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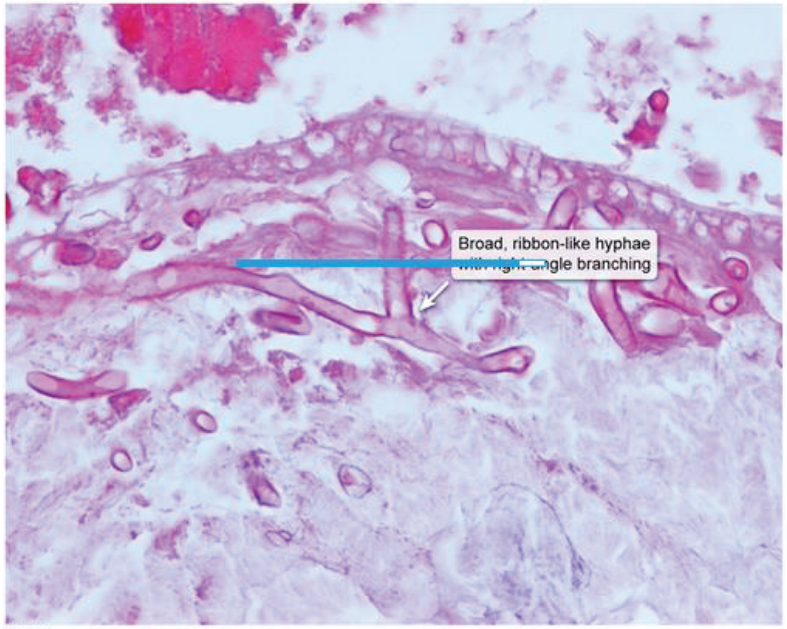
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Mucormycosis Abdominal Mucormycosis

Abdominal mucormycosis



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Researchers find that even though the current recombinant hepatitis B vaccine is immunogenic, about 10% of immunocompetent individuals do not develop high enough levels of anti-HB antibodies to confer immunity despite receiving the recommended 3 doses of the vaccine. To increase the vaccine immunogenicity, they use a lipopolysaccharide derivative as a vaccine adjuvant. The new vaccine induces an exaggerated immune response in previous nonresponders, which results in high antibody titers and, possibly, lifelong protection. Universal vaccination with the new vaccine would most likely lead to eradication of which of the following conditions?

A. Fulminant viral hepatitis
B. Hepatitis C infection
C. Hepatitis D infection
D. Hepatocellular carcinoma
E. Membranous glomerulopathy
F. Mixed cryoglobulinemia

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of immunocompetent individuals do not develop high enough levels of anti-HB antibodies to confer immunity despite receiving the recommended 3 doses of the vaccine. To increase the vaccine immunogenicity, they use a lipopolysaccharide derivative as a vaccine adjuvant. The new vaccine induces an exaggerated immune response in previous nonresponders, which results in high antibody titers and, possibly, lifelong protection. Universal vaccination with the new vaccine would most likely lead to eradication of which of the following conditions?

A. ~~Fulminant viral hepatitis~~ (6%)
B. ~~Hepatitis C infection~~ (1%)
C. Hepatitis D infection (77%)
D. Hepatocellular carcinoma (11%)
E. ~~Membranous glomerulopathy~~ (1%)
F. ~~Mixed cryoglobulinemia~~ (0%)

Correct
77%
47 secs
01/28/2021

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Hepatitis D virus (HDV) is a small, enveloped RNA virus that does not contain a replicase or RNA polymerase. Therefore, the virus is completely reliant on host cell machinery for transcription and translation. In addition, HDV is considered a **replication-defective** virus because it does not encode for viral envelope proteins, which are necessary to generate viral progeny. HDV can only finish its replication cycle in the setting of **coinfection with hepatitis B virus** (HBV). HBV encodes for several envelope proteins (HBsAg) that are used to generate the envelope of HDV. Therefore, universal vaccination against HBV would completely eliminate HDV.

HDV infection can occur as an acute coinfection with hepatitis B or as a superinfection in a chronic HBV carrier. Infection with HDV dramatically increases the already elevated risk of cirrhosis and hepatocellular carcinoma seen with HBV.

(Choice A) Fulminant viral hepatitis is rare but can occur with any of the hepatitis viruses (A, B, C, D, or E). Therefore, vaccination against HBV would not eliminate fulminant viral hepatitis.

(Choice B) There is currently no vaccine against hepatitis C virus (HCV). Vaccinating a patient against HBV would not prevent HCV infection.

(Choice D) Hepatocellular carcinoma is most commonly associated with HCV or HBV infection. Although universal vaccination against HBV would reduce the incidence of hepatocellular carcinoma, it would not

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E). Therefore, vaccination against HBV would not eliminate fulminant viral hepatitis.

(Choice B) There is currently no vaccine against hepatitis C virus (HCV). Vaccinating a patient against HBV would not prevent HCV infection.

(Choice D) Hepatocellular carcinoma is most commonly associated with HCV or HBV infection. Although universal vaccination against HBV would reduce the incidence of hepatocellular carcinoma, it would not eradicate the condition.

(Choices E and F) HBV and HCV can cause extrahepatic manifestations such as membranous glomerulopathy and mixed cryoglobulinemia due to the formation of circulating immune complexes. Although vaccination against HBV would reduce the incidence of these extrahepatic manifestations, it would not completely eliminate them.

Educational objective:
Hepatitis D virus (HDV) is a replication-defective RNA virus that is capable of causing infection only in the setting of coinfection with hepatitis B virus (HBV). HBV provides hepatitis B surface antigen for the HDV envelope.

References

- Old and new adjuvants for hepatitis B vaccines.

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A 43-year-old man undergoes induction chemotherapy for acute myeloid leukemia. Three weeks later, he is hospitalized with fever, cough, and generalized weakness. On physical examination, his temperature is 38.1 C (100.7 F), blood pressure is 102/68 mm Hg, and pulse is 125/min. The patient's pulse oximetry shows 95% on room air. Crackles are heard over the right upper lung field. His hemoglobin level is 9.5 g/dL, and leukocyte count is 900/mm^3 with an absolute neutrophil count of 100/mm^3. Chest x-ray reveals a dense infiltrate involving the right upper lung lobe. Broad-spectrum antibiotic therapy is instituted. Five days later, the patient is still febrile. Bronchoscopy with biopsy is performed and the tissue samples from the bronchoscopy grow mold. Which of the following is the most likely isolate?

A. *Aspergillus fumigatus*
B. *Candida albicans*
C. *Cryptococcus neoformans*
D. *Pneumocystis jirovecii*
E. *Rhizopus oryzae*

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is hospitalized with fever, cough, and generalized weakness. On physical examination, his temperature is 38.1 C (100.7 F), blood pressure is 102/68 mm Hg, and pulse is 125/min. The patient's pulse oximetry shows 95% on room air. Crackles are heard over the right upper lung field. His hemoglobin level is 9.5 g/dL, and leukocyte count is 900/mm^3 with an absolute neutrophil count of 100/mm^3. Chest x-ray reveals a dense infiltrate involving the right upper lung lobe. Broad-spectrum antibiotic therapy is instituted. Five days later, the patient is still febrile. Bronchoscopy with biopsy is performed and the tissue samples from the bronchoscopy grow mold. Which of the following is the most likely isolate?

- A. *Aspergillus fumigatus* (59%)
- B. *Candida albicans* (13%)
- C. *Cryptococcus neoformans* (8%)
- D. *Pneumocystis jirovecii* (13%)
- E. *Rhizopus oryzae* (5%)

Incorrect
Correct answer

59%

01 min, 02 secs

03/01/2021

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This patient with leukemia recently underwent chemotherapy (with likely myelosuppressive effects) and now has a fungal respiratory infection with **febrile neutropenia (FN)**, typically defined as fever with an **absolute neutrophil count <500/mm^3**. Patients with FN are at increased risk for severe infection. Broad-spectrum antibiotic therapy is indicated. Gram-positive organisms are now the most commonly identified pathogens in FN. However, patients with **profound and prolonged neutropenia** (several days) are at especially high risk for viral and **fungal** infections.

Invasive pulmonary aspergillosis presents with some combination of fever, chest pain, cough, dyspnea, and hemoptysis. Chest imaging can show consolidation, nodules, or cavitary lesions. On light microscopy, *Aspergillus* is seen as septate narrow hyphae that branch at a 45° angle. Antifungal therapy is needed.

(Choice B) *Candida* is another common fungal infection in patients with FN. However, respiratory infections from *Candida* are very uncommon; candidal bloodstream infections can occur in patients who have an indwelling central venous catheter.

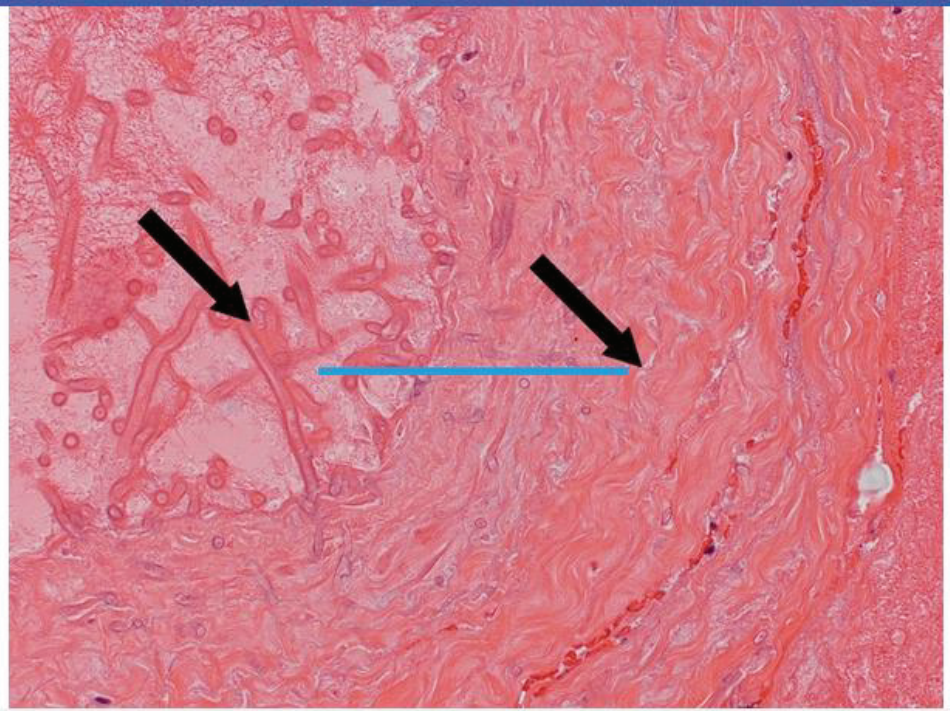
(Choice C) *Cryptococcus neoformans* is a fungus that most frequently causes opportunistic infections in patients with immunosuppression, especially those with HIV/AIDS. The most common presentation is meningoencephalitis; pneumonia is rare.

(Choice D) *Pneumocystis* pneumonia (PCP) is an important cause of severe respiratory infection in

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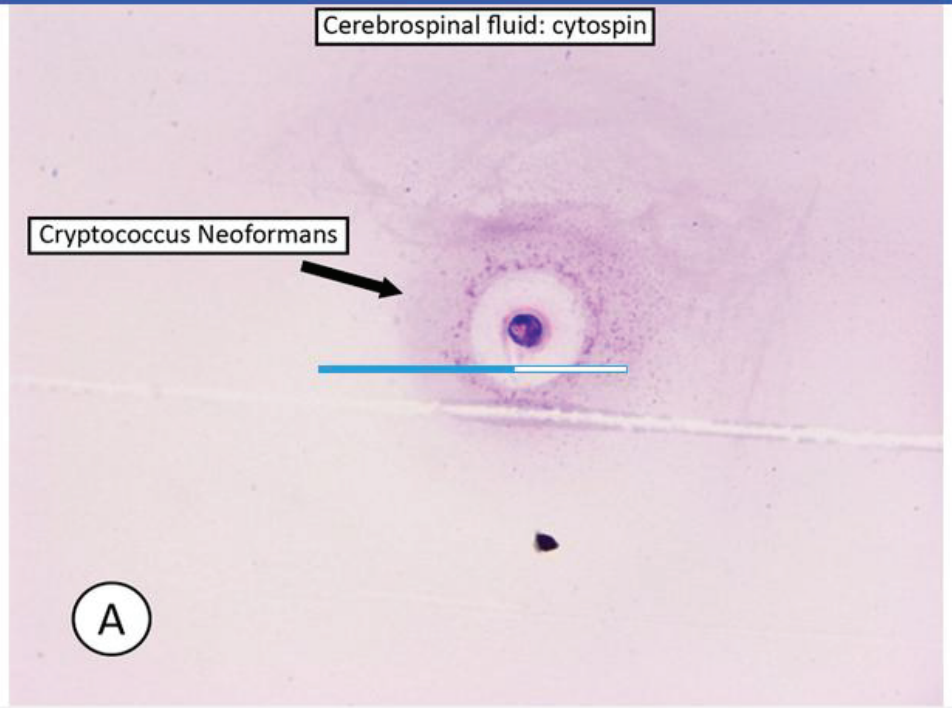
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(Choice D) *Pneumocystis* pneumonia (PCP) is an important cause of severe respiratory infection in

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(Choice D) *Pneumocystis* pneumonia (PCP) is an important cause of severe respiratory infection in

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(Choice D) *Pneumocystis* pneumonia (PCP) is an important cause of severe respiratory infection in immunocompromised patients. In patients without HIV/AIDS, PCP can present with fulminant respiratory failure, and chest radiographs reveal diffuse, bilateral interstitial infiltrates.

(Choice E) *Rhizopus* infection can lead to mucormycosis, which most commonly presents with a sinus infection that spreads rapidly to involve the orbits and brain (classically seen in patients with diabetes).

Educational objective:

Patients with profound and prolonged neutropenia are at especially high risk for viral and fungal infections. The most common fungal causes are *Aspergillus* and *Candida* species. Invasive pulmonary aspergillosis presents with some combination of fever, chest pain, cough, dyspnea, and hemoptysis.

References

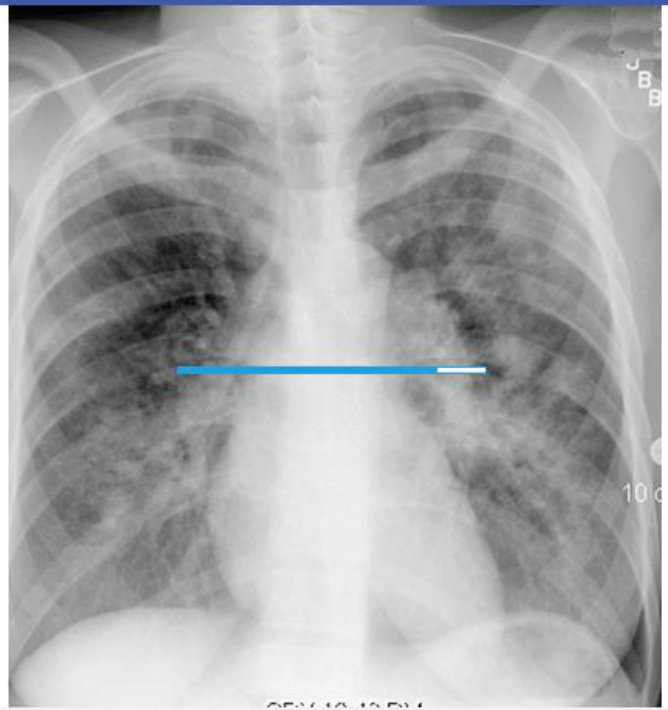
- Treatment of febrile neutropenia and prophylaxis in hematologic malignancies: a critical review and update.
- Pulmonary aspergillosis: clinical presentation, diagnostic tests, management and complications.
- Pulmonary aspergillosis: a clinical review.

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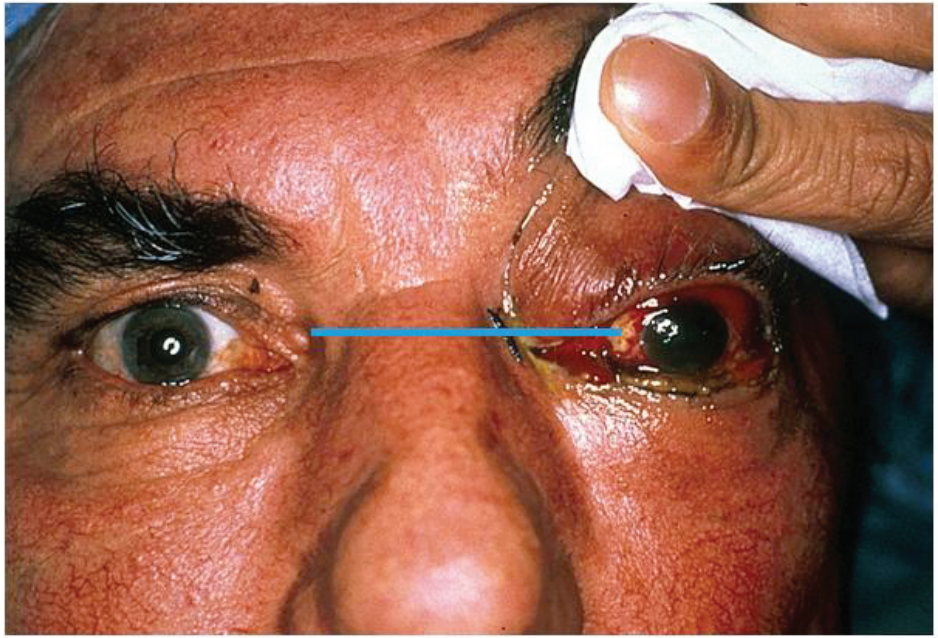


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A 31-year-old man comes to the emergency department with a 2-week history of fever, night sweats, and productive cough. He has also had a 5-kg (11-lb) weight loss. He has no other medical problems. The patient is a software engineer who moved to the United States from Uzbekistan 15 years ago. He takes no medications and has no known drug allergies. His temperature is 38.3 C (101 F), blood pressure is 110/80 mm Hg, pulse is 94/min, and respirations are 18/min. He weighs 60 kg (132.3 lb). Pulse oximetry shows 94% on room air. Chest-x ray reveals a cavitary lesion on the right. Sputum culture is obtained. When exposed to drug A, isolates of the pathogen growing in culture quickly become less resistant to decoloration with an acid-alcohol agent and stop proliferating. Which of the following is drug A most likely to be?

A. Ciprofloxacin
B. Isoniazid
C. Rifampin
D. Streptomycin
E. Vancomycin

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productive cough. He has also had a 5-kg (11-lb) weight loss. He has no other medical problems. The patient is a software engineer who moved to the United States from Uzbekistan 15 years ago. He takes no medications and has no known drug allergies. His temperature is 38.3 C (101 F), blood pressure is 110/80 mm Hg, pulse is 94/min, and respirations are 18/min. He weighs 60 kg (132.3 lb). Pulse oximetry shows 94% on room air. Chest-x ray reveals a cavitary lesion on the right. Sputum culture is obtained. When exposed to drug A, isolates of the pathogen growing in culture quickly become less resistant to decoloration with an acid-alcohol agent and stop proliferating. Which of the following is drug A most likely to be?

A. Ciprofloxacin (1%)
B. Isoniazid (72%)
C. Rifampin (20%)
D. Streptomycin (3%)
E. Vancomycin (2%)

72%
55 secs
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Drugs for treatment of tuberculosis		
Drug	**Mechanism of action**	**Side effects**
(R)ifampin	Inhibition of bacterial DNA-dependent RNA polymerase	GI side effects, rash, red-orange body fluids, cytopenias
(I)soniazid	Inhibition of mycolic acid synthesis	Neurotoxicity (give vitamin B_6/pyridoxine), hepatotoxicity
(P)yrazinamide	Unclear	Hepatotoxicity, hyperuricemia
(E)thambutol	Inhibition of arabinosyl transferase (?)	Optic neuropathy

GI = gastrointestinal.

Isoniazid is an antimicrobial agent that is active only against mycobacteria. Its specificity is derived from its **inhibition of mycolic acid synthesis**. Mycolic acids form long branched-chain fatty acids in the outer

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Isoniazid is an antimicrobial agent that is active only against mycobacteria. Its specificity is derived from its **inhibition of mycolic acid synthesis**. Mycolic acids form long branched-chain fatty acids in the outer portion of the mycobacterial peptidoglycan cell wall; they are essential for proper **cell wall** structure and virulence factor synthesis (eg, sulfatides, wax D, cord factor). If mycobacteria are unable to synthesize mycolic acids, they cannot create proper cell walls or divide to form new cells. Mycolic acids in the cell wall cause mycobacteria to be **acid-fast** as they retain the carbolfuchsin dye and resist decoloration by an acid-alcohol decolorizing agent.

(Choice A) The fluoroquinolones (eg, ciprofloxacin) are emerging as new components of the multi-drug regimen used to treat tuberculosis. They inhibit DNA gyrase, leading to fractures in the bacterial chromosome and an inability to code for proteins necessary for survival. Fluoroquinolones would not have an immediate effect on the acid-fastness of mycobacteria.

(Choice C) Rifampin is an essential component of the multi-drug regimen used to treat active tuberculosis. Rifampin halts bacterial protein synthesis by inhibiting bacterial DNA-dependent RNA polymerase, thereby preventing DNA transcription into mRNA. Rifampin would inhibit mycobacterial growth in an in vitro culture, but it would not cause the mycobacteria to lose their acid-fastness.

(Choice D) Streptomycin is an aminoglycoside that inhibits the bacterial 30S (small) ribosomal subunit,

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(Choice D) Streptomycin is an aminoglycoside that inhibits the bacterial 30S (small) ribosomal subunit, thereby halting protein synthesis. Mycobacterial cell growth is restricted and eventually cell death results. However, the acid-fastness of the organism is not affected. Streptomycin is also indicated in the treatment of plague (caused by *Yersinia pestis*) and tularemia (caused by *Francisella tularensis*).

(Choice E) Vancomycin binds to D-alanyl-D-alanine residues, inhibiting polymerization and cross-linking of the glycopeptides forming the cell wall of gram-positive bacteria (not mycobacteria).

Educational objective:

Isoniazid is an antimycobacterial agent that specifically inhibits the synthesis of mycolic acids, which are essential components of the unique mycobacterial peptidoglycan cell wall. Without mycolic acids, the mycobacteria lose their acid-fastness and become unable to synthesize new cell walls or multiply.

References

- Drugs that inhibit mycolic acid biosynthesis in Mycobacterium tuberculosis.

Pharmacology	Infectious Diseases	Tuberculosis
Subject	System	Topic

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A 38-year-old man comes to the office due to worsening fever, chills, malaise, cough, and shortness of breath. The patient has no prior medical conditions and does not use tobacco, alcohol, or illicit drugs. He has not traveled recently or been exposed to sick contacts. Temperature is 39.4 C (103 F). There is dullness to percussion and crackles over the right lung. Leukocyte count is elevated, and chest x-ray reveals a right lung infiltrate. The underlying immune response to this patient's infection largely involves T helper (Th1) cells, interferon-gamma, and interleukin-2. Which of the following is the most likely pathogen responsible for this patient's pneumonia?

A. *Haemophilus influenzae*
B. *Legionella pneumophila*
C. *Pseudomonas aeruginosa*
D. *Staphylococcus aureus*
E. *Streptococcus pneumoniae*

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A 38-year-old man comes to the office due to worsening fever, chills, malaise, cough, and shortness of breath. The patient has no prior medical conditions and does not use tobacco, alcohol, or illicit drugs. He has not traveled recently or been exposed to sick contacts. Temperature is 39.4 C (103 F). There is dullness to percussion and crackles over the right lung. Leukocyte count is elevated, and chest x-ray reveals a right lung infiltrate. The underlying immune response to this patient's infection largely involves T helper (Th1) cells, interferon-gamma, and interleukin-2. Which of the following is the most likely pathogen responsible for this patient's pneumonia?

- A. *Haemophilus influenzae* (6%)
- ✓ B. *Legionella pneumophila* (35%)
- C. *Pseudomonas aeruginosa* (3%)
- D. *Staphylococcus aureus* (6%)
- E. *Streptococcus pneumoniae* (48%)

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This patient has high fever, cough, leukocytosis, and a right lung infiltrate indicating **lobar pneumonia**. Lobar pneumonia is most commonly caused by extracellular bacterial pathogens such as *Haemophilus influenzae, Staphylococcus aureus*, and *Streptococcus pneumoniae* **(Choices A, D, and E)**. The immune response to extracellular organisms is primarily mediated by neutrophils early in infection and by the humoral antibody response (B lymphocytes, immunoglobulins, complement) as time goes on.

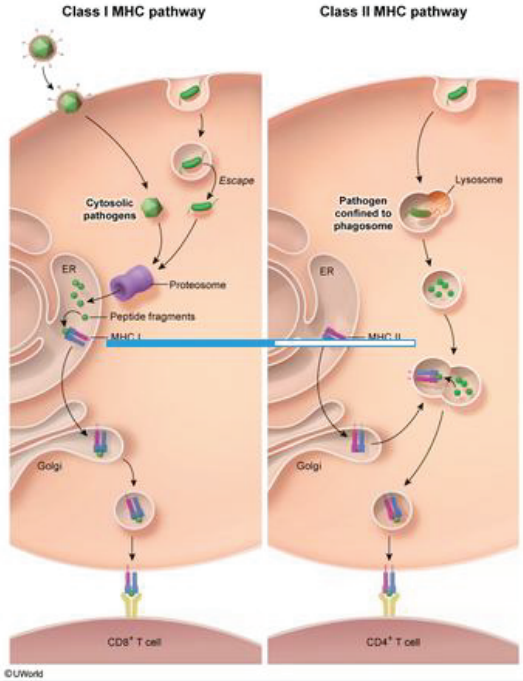
In this case, components of the **cell-mediated immune response** were primarily involved in controlling the infection, suggesting that the pneumonia was most likely due to an **intracellular pathogen** such as ***Legionella pneumophila*** (a common cause of atypical community-acquired pneumonia). Intracellular pathogens are phagocytosed by macrophages but are initially resistant to destruction due to the presence of virulence factors that inhibit phagosome-lysosome fusion (eg, *Legionella*) or phagolysosome acidification (eg, *Mycobacteria tuberculosis*), or allow bacteria to escape from the phagolysosome (eg, *Listeria monocytogenes*).

Legionella and other intracellular pathogens that initially replicate within the phagosome eventually undergo some degree of digestion by lysosomes, leading to the display of bacterial antigens on major histocompatibility complex (MHC) class II molecules. This stimulates naïve CD4 T lymphocytes to differentiate into **T-helper subtype 1 (Th1) cells**. Th1 cells release **interferon-gamma**, which activates

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differentiate into **T-helper subtype 1 (Th1) cells**. Th1 cells release **interferon-gamma**, which activates

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some degree of digestion by lysosomes, leading to the display of bacterial antigens on major histocompatibility complex (MHC) class II molecules. This stimulates naïve CD4 T lymphocytes to differentiate into **T-helper subtype 1 (Th1) cells**. Th1 cells release **interferon-gamma**, which activates macrophages and allows them to form fully mature (acidified) phagolysosomes capable of efficiently killing the intracellular bacteria. Th1 cells also release **interleukin-2**, which activates and expands the population of naïve T cells, Th1 cells, and memory T cells.

(Choice C) *Pseudomonas aeruginosa* is a common cause of pneumonia in patients who are hospitalized in the intensive care unit or those with structural lung disease such as chronic obstructive pulmonary disease. It is an extracellular pathogen primarily combated by neutrophils and the humoral immune response.

Educational objective:
Intracellular bacterial organisms such as *Legionella pneumophila* are primarily countered by the cell-mediated immune response. Intracellular pathogens that replicate within phagosomes (eg, *Legionella*, *Mycobacterium tuberculosis*) trigger activation and differentiation of T-helper subtype 1 cells with subsequent macrophage activation via interferon-gamma.

Microbiology Infectious Diseases Legionella

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An 8-year-old boy is brought to the office for rapid and irregular movements of his hands for one week. His parents say that he is also making unintentional "funny faces" and has trouble controlling the volume of his voice. His temperature is 38.9 C (102 F). On physical examination, the boy moves his hands frequently and erratically. He has a new III/VI systolic murmur and several circular, faintly erythematous lesions on his abdomen. Which of the following is the most likely mechanism for this patient's condition?

A. Nonspecific T cell receptor activation
B. Cross-reactivity of antibodies against bacterial and host antigens
C. Embolization of an infected thrombus
D. Injury from immune complex deposition
E. Release of an erythrogenic toxin

Submit

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A. Nonspecific T cell receptor activation (4%)

✓ B. Cross-reactivity of antibodies against bacterial and host antigens (71%)

C. Embolization of an infected thrombus (5%)

D. Injury from immune complex deposition (8%)

E. Release of an erythrogenic toxin (10%)

Correct

71% Answered correctly

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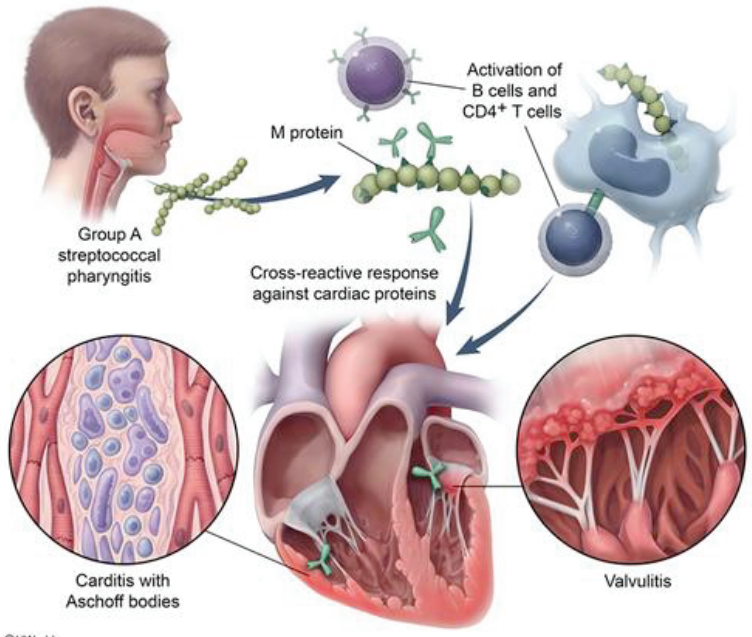
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Pathophysiology of acute rheumatic fever



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This patient has acute rheumatic fever, an immune-mediated disease following an untreated **group A streptococcal** (GAS) infection. Antibodies against GAS **cross-react** with host tissues due to **molecular mimicry** between GAS antigens and cardiac and central nervous system antigens. Specifically, antibodies directed against GAS antigens, **M protein** and **N-acetyl-beta-D-glucosamine**, subsequently attack myosin, a cardiac protein, and lysoganglioside, a neuronal cell surface protein.

The major manifestations of acute rheumatic fever include arthritis, pancarditis, Sydenham chorea, erythema marginatum, and subcutaneous nodules. This patient's murmur is likely due to acute **mitral regurgitation** from pancarditis. **Sydenham chorea** presents with non-rhythmic movements of the hands, feet, and face. Patients often have sudden changes in voice pitch and volume. Erythema marginatum presents as faintly erythematous, circular lesions with central clearing that come and go on the trunk and extremities.

(Choice A) Superantigens cause a tremendous release of cytokines through nonspecific T cell receptor activation, leading to acute fever, hypotension, and erythroderma. This is the mechanism of action of the toxic shock syndrome exotoxins produced by both *Staphylococcus aureus* and *Streptococcus pyogenes*.

(Choice C) An embolic stroke from infective endocarditis can present with fever, a new-onset murmur, and

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Acute rheumatic fever	
Epidemiology	• Endemic in developing countries
Pathogenesis	• Occurs 2-4 weeks after acute group A streptococcal pharyngitis • Molecular mimicry: Anti-streptococcal antibodies attack cardiac & neuronal antigens
Clinical features	• Acute/subacute ◦ Migratory arthritis ◦ Pancarditis (mitral regurgitation) ◦ Sydenham chorea • Chronic ◦ Mitral stenosis
Prevention	• Prompt treatment of streptococcal pharyngitis with penicillin

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(Choice C) An embolic stroke from infective endocarditis can present with fever, a new-onset murmur, and focal neurologic deficits. In addition, Janeway lesions, Osler nodes, and Roth spots are specific findings of infectious endocarditis. The most common pathogens are *S aureus*, viridans group streptococci, and enterococci.

(Choice D) The deposition of streptococcal antigen immune complexes in glomeruli causes post-streptococcal glomerulonephritis, a type III hypersensitivity reaction. Patients have microscopic or gross hematuria, edema, hypertension, and proteinuria.

(Choice E) Scarlet fever is caused by the body's response to an erythrogenic (pyrogenic) toxin released by group A *Streptococcus*. It presents with a diffuse, erythematous, "sandpaper"-textured rash most notable in the skin folds (eg, inguinal, axillary, antecubital areas). Scarlet fever can occur with pharyngitis and can lead to acute rheumatic fever if untreated.

Educational objective:

Acute rheumatic fever is an autoimmune reaction following an untreated group A streptococcal pharyngitis. Anti-group A *Streptococcus* antibodies (eg, anti-M protein, anti-N-acetyl-beta-D-glucosamine) cross-react and attack cardiac and central nervous system antigens.

References

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A 3-year-old boy is brought to the emergency department due to high fever, vomiting, and lethargy. His symptoms started 1 day ago but rapidly worsened over the last few hours. Physical examination shows hypotension, tachycardia, neck stiffness, and a petechial rash over the trunk and lower extremities. Laboratory results are as follows:

Complete blood count	
Hemoglobin	12.0 g/L
Platelets	80,000/mm^3
Leukocytes	34,500/mm^3
Neutrophils	66%
Band forms	20%
Lymphocytes	14%
Chemistry panel	
Blood urea nitrogen	30 mg/dL

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Chemistry panel

Blood urea nitrogen	30 mg/dL
Serum creatinine	1.8 mg/dL
Blood glucose	50 mg/dL

While being evaluated, the patient develops apnea and asystole. Despite aggressive resuscitation efforts, the patient dies. Autopsy would most likely reveal which of the following?

A. Adrenal hemorrhage
B. Cardiac tamponade
C. Intracerebral hemorrhage
D. Necrotizing pancreatitis
E. Saddle pulmonary embolus

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Chemistry panel

Blood urea nitrogen	30 mg/dL
Serum creatinine	1.8 mg/dL
Blood glucose	50 mg/dL

While being evaluated, the patient develops apnea and asystole. Despite aggressive resuscitation efforts, the patient dies. Autopsy would most likely reveal which of the following?

- A. Adrenal hemorrhage (80%)
- B. Cardiac tamponade (2%)
- C. Intracerebral hemorrhage (11%)
- D. Necrotizing pancreatitis (2%)
- E. Saddle pulmonary embolus (3%)

Correct

80%

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10/18/2020

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Meningococcal meningitis	
Epidemiology	• *Neisseria meningitidis* • Most common in children and young adults
Pathophysiology	• Nasopharyngeal colonization • Epithelial cell invasion • Immune system evasion (eg, capsule, variable pili)
Clinical features	• Fever, headache, vomiting, severe myalgias • Petechial/purpuric rash • Altered mental status, neck stiffness
Complications	• Septic shock, multiorgan failure • Adrenal hemorrhage/insufficiency • Disseminated intravascular coagulation

This patient's rapidly worsening fever, vomiting, altered mental status, and nuchal rigidity are consistent with **meningococcal meningitis** due to infection with *Neisseria meningitidis*. Meningococcal infection

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This patient's rapidly worsening fever, vomiting, altered mental status, and nuchal rigidity are consistent with **meningococcal meningitis** due to infection with *Neisseria meningitidis*. Meningococcal infection usually occurs in children and young adults and can present acutely with rapid progression (within hours) to **meningococcemia** and **septic shock**. These patients frequently have thrombocytopenia and a petechial rash and are at risk for development of disseminated intravascular coagulation.

A serious complication of meningococcemia is **bilateral hemorrhagic infarction** of the adrenal glands, resulting in acute adrenal insufficiency (Waterhouse-Friderichsen syndrome). Manifestations include **hypoglycemia** due to cortisol deficiency as well as **hyponatremia** and **hyperkalemia** due to aldosterone deficiency. Loss of cortisol and aldosterone also contributes to worsening shock and can result in **rapid deterioration** and death despite aggressive intervention.

(Choices B and E) Both cardiac tamponade and a saddle pulmonary embolus can cause obstructive shock that results in multiorgan failure. However, shock due to these conditions is not usually associated with adrenal insufficiency, and this patient's other clinical features (eg, neck stiffness, rash) suggest meningococcal meningitis as the primary cause.

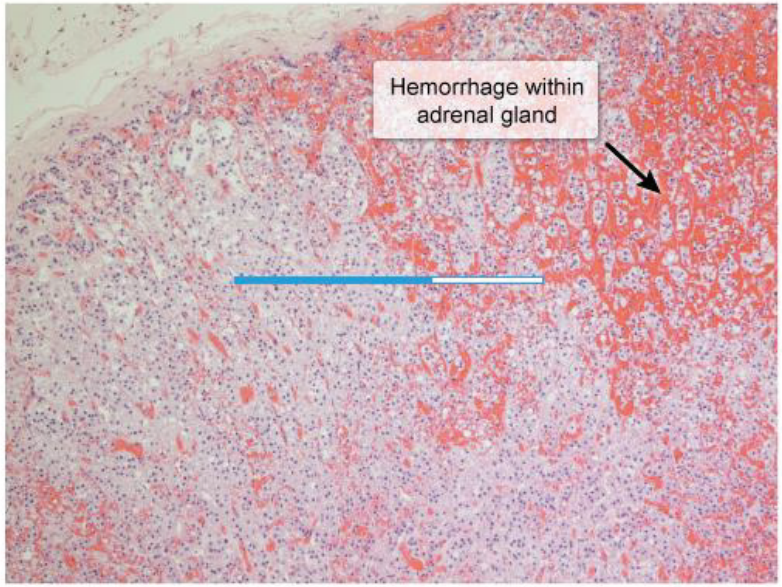
(Choice C) Intracerebral hemorrhage with increasing intracranial pressure can present with severe headache, vomiting, altered mental status, loss of consciousness, and death. Neck stiffness may be

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Waterhouse-Friderichsen syndrome



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shock that results in multiorgan failure. However, shock due to these conditions is not usually associated with adrenal insufficiency, and this patient's other clinical features (eg, neck stiffness, rash) suggest meningococcal meningitis as the primary cause.

(Choice C) Intracerebral hemorrhage with increasing intracranial pressure can present with severe headache, vomiting, altered mental status, loss of consciousness, and death. Neck stiffness may be present if the hemorrhage extends into the subarachnoid space and irritates the meninges. However, this patient's fever, petechial rash, and adrenal insufficiency make meningococcal meningitis more likely.

(Choice D) Necrotizing pancreatitis typically presents with worsening abdominal pain and vomiting, and if infected can lead to septic shock and death. However, it is not associated with neck stiffness and a petechial rash.

Educational objective:
Meningococcal meningitis is a rapidly progressive infection that can spread systemically (ie, meningococcemia) and lead to septic shock, multiorgan failure, and disseminated intravascular coagulation. Meningococcemia is also associated with bilateral hemorrhagic infarction of the adrenal glands, which can result in acute adrenal insufficiency (Waterhouse-Friderichsen syndrome) with worsening shock and rapid clinical deterioration.

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A 12-year-old boy is brought to the office with fever, chills, and a rash that appeared this morning. Two days earlier, the child started complaining of a sore throat. His temperature is 38.3 C (101 F). Examination shows a diffuse erythematous rash on his chest and abdomen that blanches with pressure, along with numerous 1- to 2-mm papules. The throat is erythematous with gray-white tonsillar exudates and the tongue is bright red. Which of the following complications is most likely to develop in this patient?

- A. Aplastic anemia
- B. Coronary artery aneurysm
- C. Encephalitis
- D. Orchitis
- E. Rheumatic fever

Submit

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A 12-year-old boy is brought to the office with fever, chills, and a rash that appeared this morning. Two days earlier, the child started complaining of a sore throat. His temperature is 38.3 C (101 F). Examination shows a diffuse erythematous rash on his chest and abdomen that blanches with pressure, along with numerous 1- to 2-mm papules. The throat is erythematous with gray-white tonsillar exudates and the tongue is bright red. Which of the following complications is most likely to develop in this patient?

- A. Aplastic anemia (2%)
- B. Coronary artery aneurysm (16%)
- C. Encephalitis (10%)
- D. ~~Orchitis~~ (6%)
- ✓ E. Rheumatic fever (63%)

Correct

63%
Answered correctly

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This patient most likely has scarlet fever, which is caused by strains of **Group A streptococcus** that produce pyrogenic exotoxins. Scarlet fever is most often associated with streptococcal **pharyngitis**, which begins acutely after an incubation period of 1-5 days. Initial symptoms include fever, malaise, abdominal pain, and sore throat. The pharynx is typically erythematous, swollen, and possibly covered with gray-white exudates. In addition, the tongue can have inflamed red papillae with an appearance similar to that of a red strawberry.

After 1-2 days, a rash appears on the neck, armpits, and groin that subsequently generalizes to the rest of the body. The rash begins as scarlet spots or blotches, giving a boiled lobster appearance. As the rash progresses and becomes more widespread, it begins to resemble a sunburn with goose pimples ("**sandpaper-like**" rash). The cheeks commonly appear flushed, giving the area around the mouth a pale appearance in comparison (circumoral pallor). Toward the end of the first week, desquamation begins and is most pronounced in the armpits, groin, and tips of the fingers and toes.

As with any streptococcal upper respiratory infection, scarlet fever can predispose to **acute rheumatic fever** and **glomerulonephritis**. Treatment with penicillin V can prevent the development of rheumatic fever, although its role in preventing glomerulonephritis is uncertain.

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Erythematous childhood rashes

Disease	Agent	Clinical presentation	Important complications
Chickenpox	Varicella-zoster virus	• **Pruritic, vesicular rash** on face, trunk & extremities • Lesions in different stages of development	Shingles (in adulthood)
Erythema infectiosum	Parvovirus B19	• Malar rash with "slapped cheek" appearance	Aplastic crisis in sickle cell and immunocompromised patients
German measles (rubella)	Rubella virus	• Maculopapular rash starting on head, progressing to trunk & extremities • **Occipital and postauricular lymphadenopathy**	Congenital rubella syndrome
Measles (rubeola)	Measles virus	• Maculopapular rash starting on head that progresses to trunk & extremities • Rash preceded by cough, coryza, conjunctivitis & **Koplik spots** (pathognomonic)	Bronchopneumonia, encephalitis
Roseola infantum	HHV 6	• High fever for 3-5 days with **rash appearing once fever subsides** • Macules & papules initially on trunk that spread to extremities	Self-limited
Scarlet fever	*Streptococcus pyogenes*	• **Sandpaper-like rash** that begins on the neck & upper trunk & then generalizes • Associated with fever & sore throat	Rheumatic fever, glomerulonephritis

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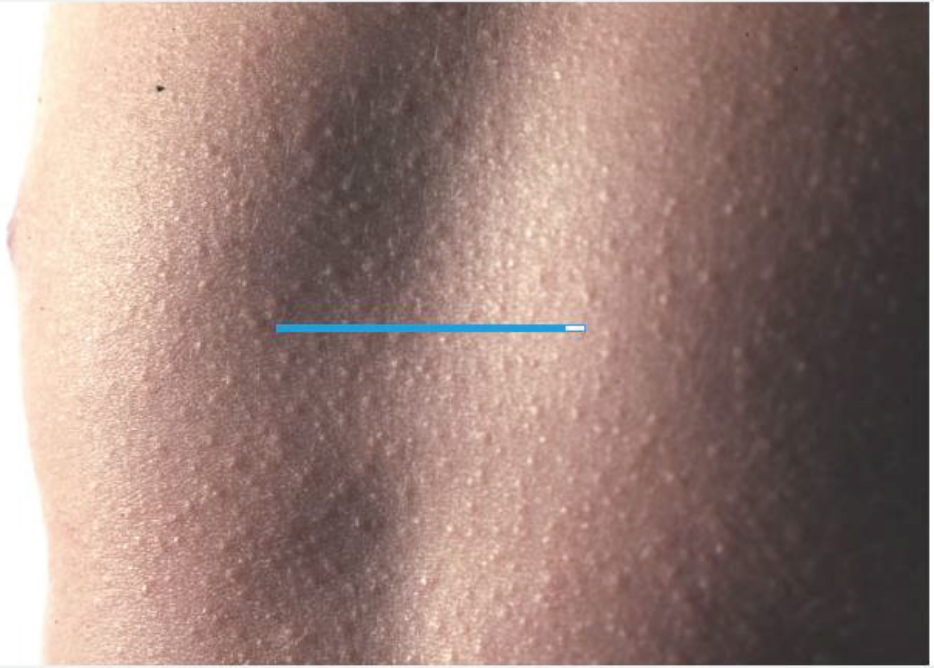
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Scarlet fever sandpaper-like rash



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Scarlet fever sandpaper-like rash



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(Choice A) Aplastic anemia can complicate parvovirus B19 infection in patients with sickle cell anemia or immunocompromisation.

(Choice B) Coronary artery aneurysm is the most dreaded complication of Kawasaki disease, which can present with fever, strawberry tongue, and a rash. However, tonsillar exudates are more typical of bacterial disease, and this patient lacks other manifestations of Kawasaki disease (eg, bilateral conjunctival injection).

(Choice C) Measles virus infection is associated with a rash that classically starts on the face and Koplik spots (small whitish/blue lesions on buccal mucosa). Neurological complications can include encephalitis (acutely), acute disseminated encephalomyelitis (during recovery), and subacute sclerosing panencephalitis (years later).

(Choice D) Orchitis is one of the most common complications of mumps. Mumps characteristically presents with fever, malaise, headaches, and myalgias followed by the development of parotitis within 48 hours.

Educational objective:
Scarlet fever is characterized by fever, pharyngitis, sandpaper-like rash, circumoral pallor, and a strawberry tongue. It is caused by strains of Group A streptococcus that produce pyrogenic exotoxins. Scarlet fever

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injection).

(Choice C) Measles virus infection is associated with a rash that classically starts on the face and Koplik spots (small whitish/blue lesions on buccal mucosa). Neurological complications can include encephalitis (acutely), acute disseminated encephalomyelitis (during recovery), and subacute sclerosing panencephalitis (years later).

(Choice D) Orchitis is one of the most common complications of mumps. Mumps characteristically presents with fever, malaise, headaches, and myalgias followed by the development of parotitis within 48 hours.

Educational objective:
Scarlet fever is characterized by fever, pharyngitis, sandpaper-like rash, circumoral pallor, and a strawberry tongue. It is caused by strains of Group A streptococcus that produce pyrogenic exotoxins. Scarlet fever can predispose to acute rheumatic fever and glomerulonephritis.

Microbiology	Infectious Diseases	Scarlet fever
Subject	System	Topic

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A 56-year-old man hospitalized in the intensive care unit is being evaluated for fever. He was admitted 8 days ago with respiratory failure and has had a complicated hospital course, including mechanical ventilation, central venous line placement, and broad-spectrum antibiotic therapy. The patient has a history of HIV and a hematologic malignancy. His last chemotherapy session was 2 weeks ago. Chest x-ray does not reveal a new infiltrate, and urine cultures are negative for infection. Blood cultures grow pseudohyphae-producing yeast species with an ability to form germ tubes. Which of the following most likely directly contributed to the development of fungemia in this patient?

A. Complement deficiency
B. Hypogammaglobulinemia
C. Low eosinophil count
D. Low neutrophil count
E. Low T-lymphocyte count

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A 56-year-old man hospitalized in the intensive care unit is being evaluated for fever. He was admitted 8 days ago with respiratory failure and has had a complicated hospital course, including mechanical ventilation, central venous line placement, and broad-spectrum antibiotic therapy. The patient has a history of HIV and a hematologic malignancy. His last chemotherapy session was 2 weeks ago. Chest x-ray does not reveal a new infiltrate, and urine cultures are negative for infection. Blood cultures grow pseudohyphae-producing yeast species with an ability to form germ tubes. Which of the following most likely directly contributed to the development of fungemia in this patient?

- A. ~~Complement deficiency~~ (2%)
- B. ~~Hypogammaglobulinemia~~ (4%)
- C. ~~Low eosinophil count~~ (4%)
- ✓ D. Low neutrophil count (22%)
- ✗ E. Low T-lymphocyte count (65%)

Incorrect

22%

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This patient with HIV likely has **candidemia**, a disseminated form of *Candida* infection. *Candida* exists as a single-celled budding yeast with pseudohyphae (*C albicans* also exhibits "germ tubes," hyphal structures formed when the organism is grown in a specific nutritionally rich serum). *Candida* is a component of normal human skin and mucous membrane flora and is an opportunistic pathogen (does not cause disseminated infection in healthy people). Host defense is provided by 2 immune system components with distinct functions:

1. **T lymphocytes** (in particular T_H cells) are important for prevention of **superficial** *Candida* infection (eg, oral/esophageal candidiasis, cutaneous candidiasis, *Candida* vulvovaginitis). Conditions such as HIV (low T-cell count) increase the risk of superficial candidiasis.
2. **Neutrophils** prevent the **hematogenous** spread of *Candida*. **Disseminated** candidiasis (eg, candidemia, endocarditis) is more likely in patients who are neutropenic or otherwise immunocompromised (eg, cancer with chemotherapy) and in those with inherited impairments of phagocytosis.

The interplay of these 2 components can be seen in patients with HIV. These patients frequently have superficial *Candida* infections given their low T-cell counts, but they do not typically suffer from disseminated candidiasis as a result of HIV itself. If they also have neutropenia, there is a risk for both

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The interplay of these 2 components can be seen in patients with HIV. These patients frequently have superficial *Candida* infections given their low T-cell counts, but they do not typically suffer from disseminated candidiasis as a result of HIV itself. If they also have neutropenia, there is a risk for both localized and disseminated candidiasis.

(Choice A) Deficiency of complement components C1, C2, and C4 leads to increased susceptibility to infections and systemic lupus erythematosus-like disease. Low levels of C5, C6, C7, C8, and C9 predispose individuals to infections with *Neisseria gonorrhea* and *N meningitidis*.

(Choice B) Hypogammaglobulinemia predisposes patients to bacterial infections. Neither superficial nor systemic candidiasis is associated with low gammaglobulin levels.

(Choice C) Low eosinophil counts are not associated with fungal infections.

(Choice E) This patient's HIV increases the risk of superficial *Candida* infections. However, fungemia is a disseminated rather than a localized (superficial) infection.

Educational objective:
Local defense against *Candida* is performed by T cells, whereas systemic infection is prevented by neutrophils. For this reason, localized candidiasis is common in patients who have HIV, but neutropenic

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disseminated candidiasis as a result of HIV itself. If they also have neutropenia, there is a risk for both localized and disseminated candidiasis.

(Choice A) Deficiency of complement components C1, C2, and C4 leads to increased susceptibility to infections and systemic lupus erythematosus-like disease. Low levels of C5, C6, C7, C8, and C9 predispose individuals to infections with *Neisseria gonorrhea* and *N meningitidis*.

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(Choice E) This patient's HIV increases the risk of superficial *Candida* infections. However, fungemia is a disseminated rather than a localized (superficial) infection.

Educational objective:

Local defense against *Candida* is performed by T cells, whereas systemic infection is prevented by neutrophils. For this reason, localized candidiasis is common in patients who have HIV, but neutropenic individuals are more likely to have the systemic form of the disease.

References

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A 43-year-old woman comes to the emergency department due to low-grade fevers and malaise. She has a history of lung transplantation due to cystic fibrosis and had 2 episodes of cytomegalovirus (CMV) viremia over the past few months, which were treated with ganciclovir. Temperature is 37.6 C (99.7 F). Physical examination is unrevealing. Chest x-ray and urinalysis are negative for infection. Polymerase chain reaction testing for CMV in blood shows elevated CMV levels consistent with CMV viremia. Given the recurrent episodes of viremia, genotype analysis is performed and demonstrates ganciclovir-resistant CMV. The patient is started on an alternate intravenous antiviral agent. She develops hypocalcemia and hypomagnesemia. Which of the following agents is the most likely cause of these side effects?

A. Acyclovir
B. Cidofovir
C. Foscarnet
D. Lamivudine
E. Sofosbuvir
F. Valganciclovir

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over the past few months, which were treated with ganciclovir. Temperature is 37.6 C (99.7 F). Physical examination is unrevealing. Chest x-ray and urinalysis are negative for infection. Polymerase chain reaction testing for CMV in blood shows elevated CMV levels consistent with CMV viremia. Given the recurrent episodes of viremia, genotype analysis is performed and demonstrates ganciclovir-resistant CMV. The patient is started on an alternate intravenous antiviral agent. She develops hypocalcemia and hypomagnesemia. Which of the following agents is the most likely cause of these side effects?

A. Acyclovir (6%)
B. Cidofovir (8%)
C. Foscarnet (73%)
D. Lamivudine (4%)
E. Sofosbuvir (1%)
F. Valganciclovir (5%)

Correct

73%
Answered correctly

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Foscarnet is a pyrophosphate analog that is sometimes used for ganciclovir-resistant cytomegalovirus (CMV) infections. Foscarnet can **chelate calcium**. Moreover, foscarnet-induced renal wasting of magnesium may lead to **hypomagnesemia** and a reduction in the release of parathyroid hormone, which contributes to the hypocalcemic state. Both hypocalcemia and hypomagnesemia can promote **seizures**.

(Choice A) Major toxicities of acyclovir (used in some herpes simplex virus infections) include crystal nephropathy and neurotoxicity that manifests as delirium and/or tremor.

(Choice B) Cidofovir, used in some cases of CMV retinitis, is associated with nephrotoxicity manifesting as proteinuria or elevated creatinine.

(Choice D) Lamivudine is a nucleoside reverse transcriptase inhibitor (NRTI). Side effects are unusual with lamivudine, unlike other NRTIs. Lamivudine is occasionally associated with peripheral neuropathy and lactic acidosis.

(Choice E) Sofosbuvir inhibits nonstructural protein 5B (NS5B), an RNA-dependent RNA polymerase needed for hepatitis C virus replication. Adverse effects associated with its use include fatigue and nausea.

(Choice F) Valganciclovir is a ganciclovir prodrug and is unlikely to be useful against ganciclovir-resistant CMV. Ganciclovir is associated with severe neutropenia, which can be exacerbated by other bone-marrow

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(Choice E) Sofosbuvir inhibits nonstructural protein 5B (NS5B), an RNA-dependent RNA polymerase needed for hepatitis C virus replication. Adverse effects associated with its use include fatigue and nausea.

(Choice F) Valganciclovir is a ganciclovir prodrug and is unlikely to be useful against ganciclovir-resistant CMV. Ganciclovir is associated with severe neutropenia, which can be exacerbated by other bone-marrow suppressing agents (eg, zidovudine, trimethoprim-sulfamethoxazole).

Educational objective:
Foscarnet is an analog of pyrophosphate that can chelate calcium and promote nephrotoxic renal magnesium wasting. These toxicities can result in hypocalcemia and hypomagnesemia, which can cause seizures.

Pharmacology	Infectious Diseases	Foscarnet
Subject	System	Topic

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A 65-year-old man comes to the emergency department with a sore on his right hand. The lesion began as a small, painless papule 3 days ago and rapidly enlarged and ulcerated. The patient has had no injury or insect bite, has no prior medical conditions, and takes no medications. He is in the wool business and recently returned from a tour of wool-processing plants in several Asian countries. Physical examination shows a necrotic ulcer with a black eschar on the dorsum of the right hand. There is extensive edema of surrounding tissues. The toxin causing edema around this patient's ulcer has a mechanism of action most similar to a different toxin produced by which of the following bacteria?

A. *Bordetella pertussis*
B. *Clostridium botulinum*
C. *Clostridium difficile*
D. *Shigella dysenteriae*
E. *Streptococcus pyogenes*

Submit

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- A. *Bordetella pertussis* (64%)
- B. *Clostridium botulinum* (6%)
- C. *Clostridium difficile* (12%)
- D. *Shigella dysenteriae* (6%)
- E. *Streptococcus pyogenes* (10%)

64% 01 min, 18 secs 01/08/2021

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Mechanism of action of selected bacterial exotoxins		
Organism	**Toxin**	**Mechanism & effects**
Bacillus anthracis	Anthrax exotoxin	Edema factor: Increases cyclic AMP concentration by acting as an adenylate cyclase, causing edema & phagocyte dysfunction
		Lethal factor: Zinc-dependent protease that inhibits mitogen-activated protein kinase signaling, causing apoptosis & multisystem physiologic disruption
Bordetella pertussis	Pertussis toxin	Disinhibits adenylate cyclase through G_i ADP-ribosylation, increasing cAMP levels; causes edema & phagocyte dysfunction
	Adenylate cyclase toxin	Functions as an adenylate cyclase, increasing cAMP levels; causes edema & phagocyte dysfunction
Clostridium botulinum	Botulinum toxin	Blocks presynaptic release of acetylcholine at the neuromuscular junction, resulting in flaccid paralysis

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	cyclase toxin	causes edema & phagocyte dysfunction
Clostridium botulinum	Botulinum toxin	Blocks presynaptic release of acetylcholine at the neuromuscular junction, resulting in flaccid paralysis
Clostridium difficile	Toxin A	Recruits & activates neutrophils, leading to release of cytokines that cause mucosal inflammation, fluid loss & diarrhea
	Toxin B	Induces actin depolymerization, leading to mucosal cell death, bowel wall necrosis & pseudomembrane formation
Shigella dysenteriae	Shiga toxin	Halts protein synthesis by disabling the 60S ribosomal subunit, leading to intestinal epithelial cell death & diarrhea
Streptococcus pyogenes	Pyrogenic exotoxin	Acts as a superantigen, inducing fever & shock; associated with scarlet fever & streptococcal toxic shock syndrome
	Streptolysin O&S	Damages erythrocyte membranes, causing beta hemolysis

Bacillus anthracis is a gram-positive, sporulating bacterium that primarily affects herbivores (eg, sheep, cows) that graze on contaminated pastures. However, transmission to humans can occasionally occur due

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Bacillus anthracis is a gram-positive, sporulating bacterium that primarily affects herbivores (eg, sheep, cows) that graze on contaminated pastures. However, transmission to humans can occasionally occur due to inhalation, ingestion, or cutaneous inoculation of *B anthracis* spores. Risk is greatest in those who handle contaminated hides, animal hair (eg, wool), or carcasses. Cutaneous exposure usually results in a painless papule that rapidly ulcerates and subsequently turns into a black eschar.

B anthracis spores germinate at tissue temperatures into vegetative rods that have 2 main virulence factors:

- A **polypeptide capsule** composed of poly-γ-D-glutamic acid, which inhibits phagocytosis
- A **trimeric exotoxin** composed of protective antigen, edema factor, and lethal factor

Protective antigen binds to a host cell membrane receptor on macrophages and forms a channel that delivers lethal factor and edema factor into the cell. Lethal factor is a zinc metalloproteinase that inhibits MAP kinase signal transduction, leading to cell death. Edema factor is a **calmodulin-dependent adenylate cyclase** that increases cyclic AMP concentration, leading to accumulation of fluid within/between cells and suppression of neutrophil and macrophage function.

The mechanism of action of edema factor is very similar to that of the **adenylate cyclase toxin** produced

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within/between cells and suppression of neutrophil and macrophage function.

The mechanism of action of edema factor is very similar to that of the **adenylate cyclase toxin** produced by ***Bordetella pertussis***. Adenylate cyclase toxin is also a calmodulin-dependent adenylate cyclase that increases cAMP concentration, leading to edema and phagocyte dysfunction. This results in localized immunosuppression that allows *B pertussis* to colonize the respiratory tract. The other major *B pertussis* exotoxin is pertussis toxin, which increases cAMP concentration via ADP-ribosylation of a membrane G-protein.

(Choices B and C) Both *Clostridium botulinum* and *C difficile* are sporulating bacteria whose vegetative forms generate exotoxins. However, the exotoxins produced by these bacteria operate by different mechanisms than edema factor or lethal factor. Botulinum toxin is an endopeptidase that blocks neuromuscular cholinergic transmission; toxins A and B (generated by *C difficile*) inactivate Rho family proteins, leading to a derangement of cytoskeletal structure and guanosine triphosphate signal transduction.

(Choice D) *Shigella dysenteriae* invades colonic mucosal cells and produces Shiga toxin, an exotoxin that cleaves a peptide off the 60S ribosomal subunit and causes irreversible inhibition of protein synthesis.

(Choice E) *Streptococcus pyogenes* strains that have been exposed to a specific lysogenic bacteriophage

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proteins, leading to a derangement of cytoskeletal structure and guanosine triphosphate signal transduction.

(Choice D) *Shigella dysenteriae* invades colonic mucosal cells and produces Shiga toxin, an exotoxin that cleaves a peptide off the 60S ribosomal subunit and causes irreversible inhibition of protein synthesis.

(Choice E) *Streptococcus pyogenes* strains that have been exposed to a specific lysogenic bacteriophage produce pyrogenic exotoxins, which cause scarlet fever and streptococcal toxic shock syndrome. These exotoxins are proteases that degrade host cell proteins or nonspecifically activate T cells (superantigens).

Educational objective:

Bacillus anthracis edema factor is an adenylate cyclase that increases intracellular cyclic AMP, leading to neutrophil and macrophage dysfunction and tissue edema. This mechanism of action is similar to that of adenylate cyclase toxin, produced by *Bordetella pertussis*.

References

- Cellular and physiological effects of anthrax exotoxin and its relevance to disease.
- Pertussis toxin and adenylate cyclase toxin: key virulence factors of Bordetella pertussis and cell biology tools.
- The adenylate cyclase toxins.

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www.ncbi.nlm.nih.gov/pubmed/15490970

A 28-year-old man comes to the office due to a rash. He has a history of seizure disorder and has been taking phenytoin for 6 years. Examination shows a diffuse, macular rash and lymphadenopathy. Biopsy of a lymph node is shown in the exhibit. Treatment of this patient's condition is most likely to involve which of the following?

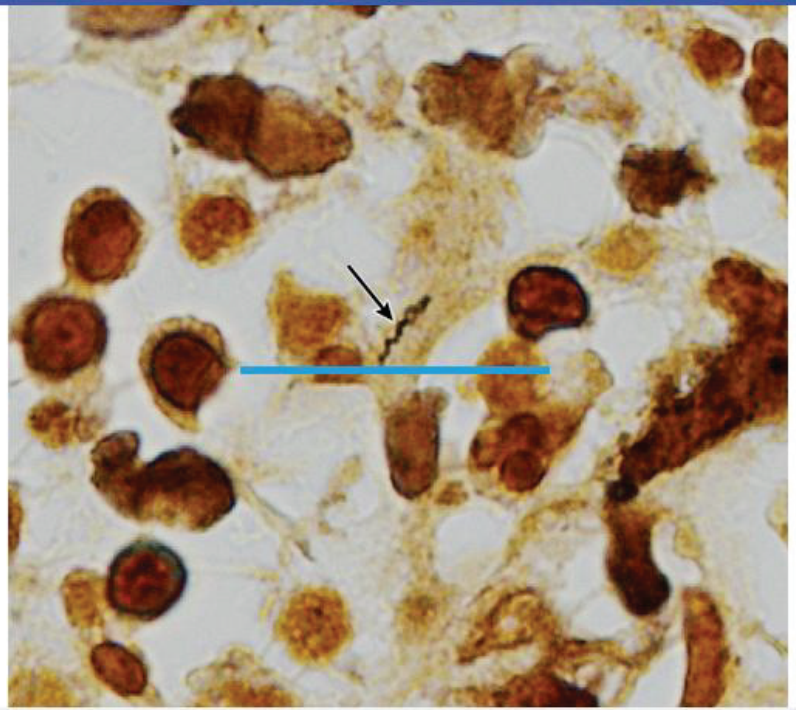
A. Blockade of viral reverse transcriptase and integrase
B. Diminished type IV delayed hypersensitivity reaction
C. Inhibition of bacterial DNA gyrase and topoisomerase
D. Inhibition of transpeptidase and bacterial cell wall cross-linking
E. Reduced production of dihydrofolic acid and tetrahydrofolic acid

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A 28-year-old man comes to the office due to a rash. He has a history of seizure disorder and has been taking phenytoin for 6 years. Examination shows a diffuse, macular rash and lymphadenopathy. Biopsy of a lymph node is shown in the exhibit. Treatment of this patient's condition is most likely to involve which of the following?

A. ~~Blockade of viral reverse transcriptase and integrase~~ (4%)
B. ~~Diminished type IV delayed hypersensitivity reaction~~ (10%)
C. ~~Inhibition of bacterial DNA gyrase and topoisomerase~~ (14%)
✓ D. Inhibition of transpeptidase and bacterial cell wall cross-linking (56%)
E. Reduced production of dihydrofolic acid and tetrahydrofolic acid (15%)

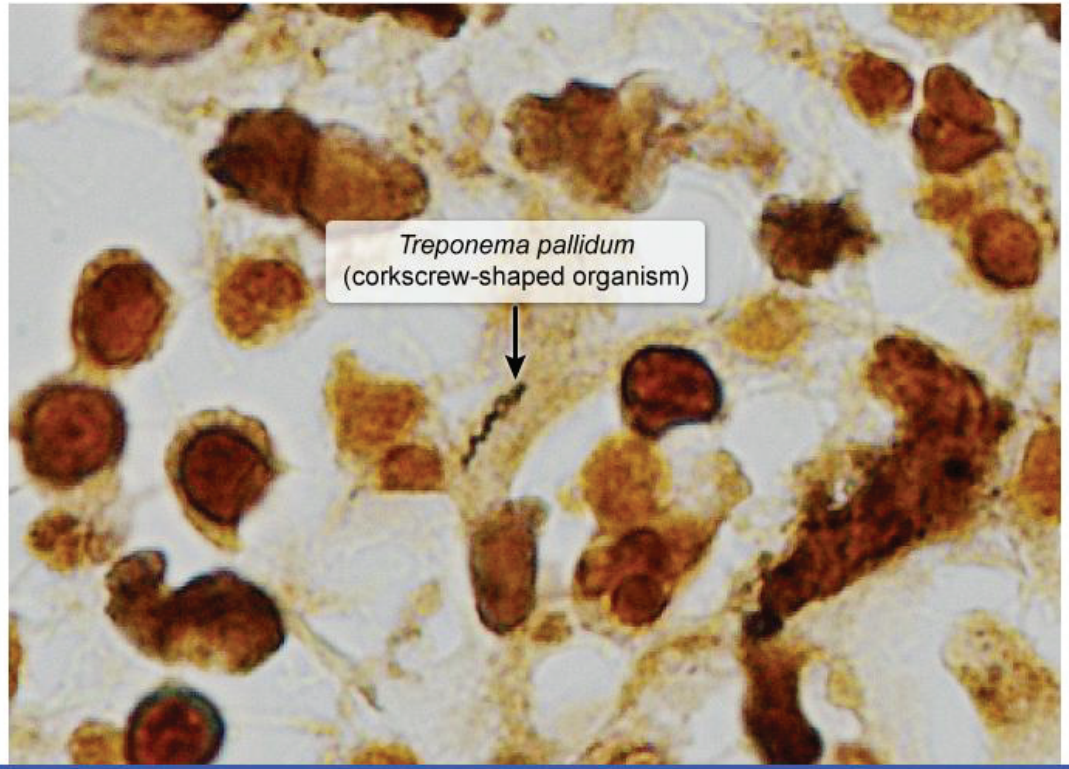
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Explanation

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Syphilis



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The presence of a generalized rash, lymphadenopathy, and a **corkscrew-shaped organism** on histopathology suggests **secondary syphilis**, a spirochetal infection caused by *Treponema pallidum*. Inoculation occurs via skin-to-skin contact during sexual intercourse; replication of *T pallidum* at the site of transmission results in an ulcer with heaped up borders (primary syphilis). Subsequent spread through the dermal lymphatic system leads to systemic spread.

Secondary syphilis develops in untreated patients weeks or months after the chancre has resolved. Common manifestations include a **diffuse, macular rash** and **generalized lymphadenopathy**. The diagnosis is generally made with nontreponemal (eg, rapid plasma reagin) and treponemal-specific (eg, fluorescent treponemal antibody absorption) serologic testing because microscopy is technically difficult and less sensitive. However, **dark-field microscopy** or specialized silver stains can identify the spirochete.

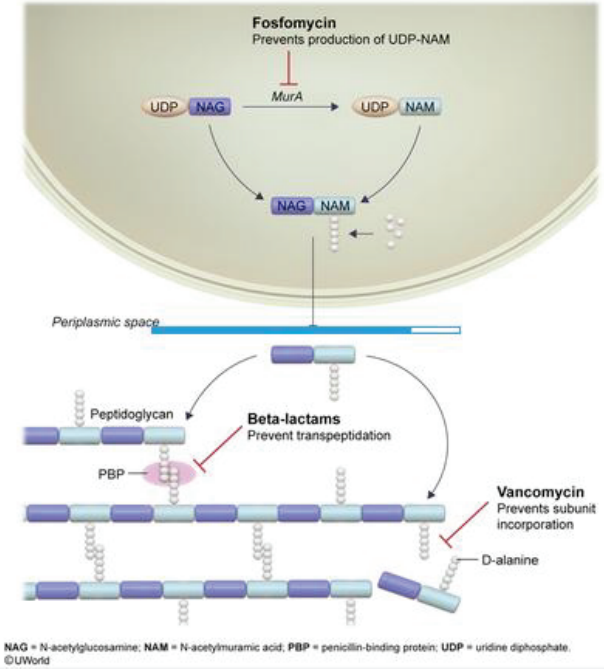
All stages of syphilis are most effectively treated with **penicillin**, a beta-lactam antibiotic that disrupts cell wall synthesis by **inhibiting** transpeptidase, a bacterial enzyme necessary for **cell wall cross-linking**. Because penicillin is effective only against bacteria that are dividing, and because *T pallidum* replicates slowly, penicillin preparations that provide prolonged exposure (eg, intramuscular penicillin G benzathine) are required.

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Exhibit Display

Antibiotics that inhibit cell wall synthesis



NAG = N-acetylglucosamine; **NAM** = N-acetylmuramic acid; **PBP** = penicillin-binding protein; **UDP** = uridine diphosphate.
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are required.

(Choice A) HIV is typically treated with reverse transcriptase and integrase inhibitors. Although acute HIV infection often presents with rash, lymphadenopathy, and constitutional symptoms a few weeks after transmission, a spiral-shaped organism would not be seen on biopsy.

(Choice B) Phenytoin can cause a diffuse rash due to a delayed type IV hypersensitivity reaction. However, most cases arise within a few weeks of initiating therapy, not 6 years later. In addition, a corkscrew-shaped organism would not be seen on biopsy.

(Choice C) Fluroquinolones (eg, ciprofloxacin) disrupt bacterial DNA synthesis by blocking bacterial DNA gyrase and topoisomerase. Fluroquinolones are often used for gram-negative bacterial infections (eg, urinary tract infection) but not for syphilis.

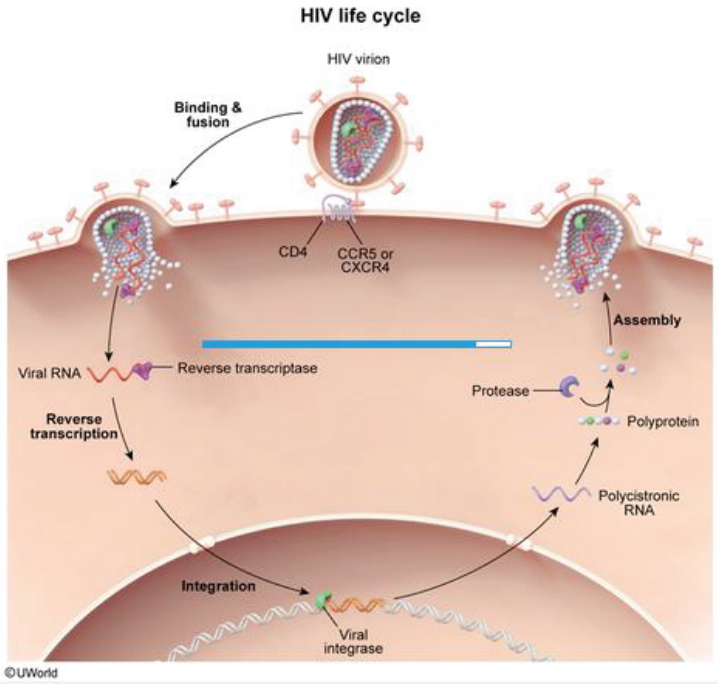
(Choice E) Trimethoprim-sulfamethoxazole disrupts bacterial folate metabolism by blocking enzymes that generate dihydrofolic and tetrahydrofolic acid. This agent is often used for urinary tract and skin/soft tissue infection but is not used for syphilis.

Educational objective:
Syphilis is caused by the corkscrew-shaped organism *Treponema pallidum*. Secondary syphilis develops in untreated patients weeks or months after the initial infection, and presents with a diffuse, macular rash

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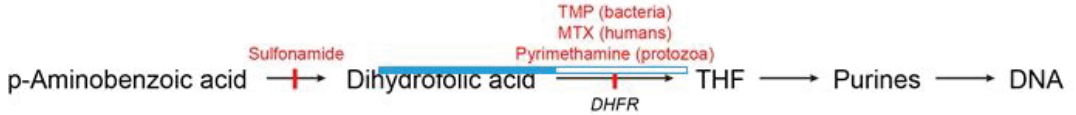
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Trimethoprim-sulfamethoxazole & folic acid pathway



DHFR = dihydrofolate reductase; MTX = methotrexate; THF = tetrahydrofolic acid; TMP = trimethoprim

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corkscrew-shaped organism would not be seen on biopsy.

(Choice C) Fluroquinolones (eg, ciprofloxacin) disrupt bacterial DNA synthesis by blocking bacterial DNA gyrase and topoisomerase. Fluroquinolones are often used for gram-negative bacterial infections (eg, urinary tract infection) but not for syphilis.

(Choice E) Trimethoprim-sulfamethoxazole disrupts bacterial folate metabolism by blocking enzymes that generate dihydrofolic and tetrahydrofolic acid. This agent is often used for urinary tract and skin/soft tissue infection but is not used for syphilis.

Educational objective:

Syphilis is caused by the corkscrew-shaped organism *Treponema pallidum*. Secondary syphilis develops in untreated patients weeks or months after the initial infection, and presents with a diffuse, macular rash and generalized lymphadenopathy. First-line treatment is penicillin, which blocks the last step in bacterial cell wall synthesis (transpeptidation).

Pharmacology	Infectious Diseases	Syphilis
Subject	System	Topic

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An 18-year-old man comes to the emergency department due to 3 days of fever, myalgias, and profound fatigue. He was feeling fine prior to the onset of symptoms. The patient has a history of intermittent asthma for which he uses an inhaler as needed. He is a senior in high school and plays on the football team. Temperature is 38 C (100.4 F), blood pressure is 110/80 mm Hg, pulse is 88/min, and respirations are 16/min. BMI is 22.1 kg/m^2. On physical examination, the patient is found to have swollen lymph nodes in his neck and behind his ears. The tip of the spleen is palpable 1 cm below the left costal margin. Laboratory results are notable for the following:

Complete blood count	
Hemoglobin	14.4 g/dL
Platelets	310,000/mm^3
Leukocytes	11,000/mm^3
Lymphocytes	70%

Which of the following is most likely to be elicited on further history?

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Platelets	310,000/mm^3
Leukocytes	11,000/mm^3
Lymphocytes	70%

Which of the following is most likely to be elicited on further history?

A. Anal sexual intercourse
B. Contact with saliva
C. Exposure to urine
D. Prior blood transfusion
E. Recent tick bite
F. School trip to South Asia

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Platelets	310,000/mm^3
Leukocytes	11,000/mm^3
Lymphocytes	70%

Which of the following is most likely to be elicited on further history?

- A. Anal sexual intercourse (1%)
- ✓ B. Contact with saliva (91%)
- C. Exposure to urine (0%)
- D. Prior blood transfusion (1%)
- E. Recent tick bite (3%)
- F. School trip to South Asia (2%)

Correct

91%

01 min, 13 secs

12/11/2020

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This patient has many of the classic features of Epstein-Barr virus (**EBV**)-induced **mononucleosis**, including fever, profound fatigue, lymphadenopathy, lymphocytosis (with atypical lymphocytes), and splenomegaly (palpable spleen tip). EBV is typically transmitted from an asymptomatic virus shedder to a susceptible individual through **saliva** transfer (eg, kissing).

(Choice A) Anal sexual intercourse is more likely to transmit pathogens such as HIV, *Neisseria gonorrhoeae*, and *Chlamydia trachomatis*.

(Choices C, D, and E) Urine can harbor pathogens such as cytomegalovirus, adenovirus, *Escherichia coli, Staphylococcus saprophyticus*, and *Klebsiella pneumoniae*; blood can harbor hepatitis B virus, hepatitis C virus, and HIV; and arthropods (eg, ticks) can harbor *Rickettsia rickettsii* and *Borrelia burgdorferi*, among others.

(Choice F) Malaria and leishmaniasis, which can cause splenomegaly, are found in South Asia. However, malaria would classically be associated with anemia and thrombocytopenia. Visceral leishmaniasis (kala-azar) manifests as progressive splenic enlargement and weight loss over months.

Educational objective:
Typical clinical and laboratory features of Epstein-Barr virus (EBV) mononucleosis include fever, pharyngitis, lymphadenopathy, splenomegaly, and atypical lymphocytosis. EBV is generally transmitted

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(Choices C, D, and E) Urine can harbor pathogens such as cytomegalovirus, adenovirus, *Escherichia coli, Staphylococcus saprophyticus*, and *Klebsiella pneumoniae*; blood can harbor hepatitis B virus, hepatitis C virus, and HIV; and arthropods (eg, ticks) can harbor *Rickettsia rickettsii* and *Borrelia burgdorferi*, among others.

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Educational objective:
Typical clinical and laboratory features of Epstein-Barr virus (EBV) mononucleosis include fever, pharyngitis, lymphadenopathy, splenomegaly, and atypical lymphocytosis. EBV is generally transmitted from an asymptomatic virus shedder to a susceptible individual through saliva transfer (eg, kissing).

Microbiology	Infectious Diseases	Infectious mononucleosis
Subject	System	Topic

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A 50-year-old woman comes to the emergency department due to fever and abdominal pain. The patient has a history of type 2 diabetes mellitus. Her temperature is 38.3 C (101 F). Abdominal examination is notable for right upper quadrant tenderness to palpation that is worsened by deep inspiration. Laboratory studies show leukocytosis. An ultrasound of the abdomen reveals multiple gallstones and gallbladder wall thickening with pericholecystic fluid. Blood cultures are drawn, and surgical consultation is requested. The patient is initiated on intravenous piperacillin combined with tazobactam. Which of the following is the most likely reason to use this drug combination in this patient?

A. Decrease bacterial inactivation of piperacillin
B. Decrease renal clearance of piperacillin
C. Enhance bacterial penetration of piperacillin
D. Increase bioavailability of piperacillin
E. Provide additive antimicrobial activity

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A 50-year-old woman comes to the emergency department due to fever and abdominal pain. The patient has a history of type 2 diabetes mellitus. Her temperature is 38.3 C (101 F). Abdominal examination is notable for right upper quadrant tenderness to palpation that is worsened by deep inspiration. Laboratory studies show leukocytosis. An ultrasound of the abdomen reveals multiple gallstones and gallbladder wall thickening with pericholecystic fluid. Blood cultures are drawn, and surgical consultation is requested. The patient is initiated on intravenous piperacillin combined with tazobactam. Which of the following is the most likely reason to use this drug combination in this patient?

- A. Decrease bacterial inactivation of piperacillin (79%)
- B. Decrease renal clearance of piperacillin (2%)
- C. Enhance bacterial penetration of piperacillin (8%)
- D. Increase bioavailability of piperacillin (2%)
- E. Provide additive antimicrobial activity (6%)

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This patient's fever, leukocytosis, right upper quadrant pain with positive Murphy sign, and ultrasound findings (eg, gallstones, wall thickening, pericholecystic fluid) indicate **acute cholecystitis**. Antibiotic therapy is often administered to prevent secondary infection (eg, *Escherichia coli, Klebsiella*) due to biliary stasis, particularly in patients who have diabetes mellitus or immunodeficiency.

The penicillin family of antibiotics (eg, piperacillin) contains a **beta-lactam ring**, which inhibits peptidoglycan cross-linking and causes bacterial cell wall disruptions. Resistance is often due to **beta-lactamase**, a bacterial enzyme that hydrolyzes and inactivates the beta-lactam ring. The coadministration of a **beta-lactamase inhibitor** such as tazobactam prevents beta-lactamase producing organisms from inactivating penicillins, which extends their spectrum of activity (broadens the range of microbes that can be treated).

Some penicillin-derivative antibiotics (eg, late-generation cephalosporins, carbapenems) have beta-lactam rings with additional chemical components, which make them partially or completely resistant to beta-lactamases.

(Choice B) Probenecid, a uricosuric agent used for hyperuricemia with gout, blocks the renal tubular excretion of penicillins and cephalosporins and is sometimes used to increase their serum level or prolong

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(Choice B) Probenecid, a uricosuric agent used for hyperuricemia with gout, blocks the renal tubular excretion of penicillins and cephalosporins and is sometimes used to increase their serum level or prolong their half-life.

(Choice C) Aminoglycosides inhibit bacterial protein synthesis by blocking the 30S ribosomal subunit. Penicillins are often coadministered with aminoglycosides to aid in their entry into the cell (penicillins disrupt the cell wall, which allow aminoglycosides to penetrate the bacteria).

(Choice D) Piperacillin is always administered intravenously so bioavailability is 100%. Tazobactam inhibits beta-lactamase; it does not alter piperacillin metabolism or excretion.

(Choice E) Additive antimicrobial activity occurs when 2 different antibiotic classes are used in combination, such as a fluoroquinolone (DNA gyrase inhibitor) with vancomycin (cell wall synthesis inhibitor). Beta-lactamase inhibitors block an enzyme that destroys penicillins; they do not independently provide antimicrobial activity so they are always used in combination with penicillin-class agents.

Educational objective:
Beta-lactamase inhibitors (eg, clavulanic acid, sulbactam, tazobactam) prevent beta-lactamase from inactivating penicillin class drugs, which extends the spectrum of their activity.

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The rates of hepatocellular carcinoma in some developing countries are many times higher than that in Western nations. A successful hepatocellular carcinoma prevention strategy in these countries would focus on incorporating:

- A. Water sanitation
- B. Vitamin supplementation
- C. Universal vaccination
- D. Adequate antibiotic use
- E. Routine physician check-ups
- F. Wider access to hospital care

Submit

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The rates of hepatocellular carcinoma in some developing countries are many times higher than that in Western nations. A successful hepatocellular carcinoma prevention strategy in these countries would focus on incorporating:

- A. ~~Water sanitation~~ (9%)
- B. ~~Vitamin supplementation~~ (0%)
- ✓ C. Universal vaccination (81%)
- D. ~~Adequate antibiotic use~~ (1%)
- E. Routine physician check-ups (4%)
- F. ~~Wider access to hospital care~~ (2%)

Correct

81% Answered correctly

28 secs Time Spent

01/30/2021 Last Updated

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Worldwide, those countries with high rates of hepatitis B virus (HBV) infection have more than 85% of all hepatocellular carcinoma (HCC) cases. Korea, Taiwan, Mozambique, and China experience the highest annual rates of HCC (36 per 100,000 versus <5 per 100,000 in North America). The individuals who develop HCC in these countries usually have chronic HBV infection acquired through vertical transmission at childbirth, which increases their risk of developing HCC by early to middle adulthood 200-fold. In the United States, HCC normally arises after the age of 60. In these countries with high rates of HBV infection, however, HCC commonly presents in adults 20 to 40 years old.

Therefore, universal vaccination of children against HBV would be the one measure most likely to cause a steep decline in the incidence of hepatocellular carcinoma worldwide.

(Choice A) Improved water sanitation would be of significant help in reducing the incidence of many foodborne illnesses transmitted through the fecal-oral route (such as hepatitis A).

(Choice B) Vitamin supplementation would be of significant help in reducing the incidence of conditions associated with poor nutrition (eg, pellagra).

(Choice D) Adequate antibiotic usage would be of significant help in reducing the length and severity of bacterial infections.

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(Choice A) Improved water sanitation would be of significant help in reducing the incidence of many foodborne illnesses transmitted through the fecal-oral route (such as hepatitis A).

(Choice B) Vitamin supplementation would be of significant help in reducing the incidence of conditions associated with poor nutrition (eg, pellagra).

(Choice D) Adequate antibiotic usage would be of significant help in reducing the length and severity of bacterial infections.

(Choices E and F) Routine physician check-ups and wider access to hospital care would be of significant help in educating the patient population, identifying disease processes in early stages, and reducing suffering.

Educational Objective:
Universal vaccination of children against HBV would likely cause a steep decline in the worldwide incidence of hepatocellular carcinoma.

Pathology	Infectious Diseases	Hepatocellular cancer
Subject	System	Topic

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A 7-year-old boy is evaluated for a foot wound. He sustained a splinter injury to his left foot while playing in the yard several days ago and has continued to have purulent drainage from the wound. The patient has no significant medical history and is up to date with all recommended vaccinations. Wound examination reveals a small retained foreign body with surrounding necrotic tissue and pus. Anaerobic culture of the wound swab grows thin, gram-positive rods with terminal spore, which is biochemically identified as *Clostridium tetani*. Which of the following most likely protected this patient from developing neurological symptoms of the infection?

A. Activated macrophages capable of killing the bacteria
B. Circulating antibodies that activate complement
C. Circulating antibodies that neutralize bacterial products
D. Neutrophil infiltration of the wound with lysosomal enzyme release
E. Sensitized $CD8^+$ lymphocytes capable of killing the bacteria

Submit

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A 7-year-old boy is evaluated for a foot wound. He sustained a splinter injury to his left foot while playing in the yard several days ago and has continued to have purulent drainage from the wound. The patient has no significant medical history and is up to date with all recommended vaccinations. Wound examination reveals a small retained foreign body with surrounding necrotic tissue and pus. Anaerobic culture of the wound swab grows thin, gram-positive rods with terminal spore, which is biochemically identified as *Clostridium tetani*. Which of the following most likely protected this patient from developing neurological symptoms of the infection?

A. ~~Activated macrophages capable of killing the bacteria~~ (3%)

B. Circulating antibodies that activate complement (11%)

✓ C. Circulating antibodies that neutralize bacterial products (68%)

D. ~~Neutrophil infiltration of the wound with lysosomal enzyme release~~ (8%)

E. ~~Sensitized CD8+ lymphocytes capable of killing the bacteria~~ (8%)

68% 01 min, 13 secs 02/10/2021

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Clostridium tetani is a thin, gram-positive rod with a round terminal spore that grows in strict anaerobic conditions. It is a normal commensal of the gastrointestinal tract of many mammals and is found in soil worldwide. Transmission to humans typically occurs when *C tetani* spores are inoculated into a **skin wound**. In anaerobic conditions, the spores germinate into a vegetative rod and replicate locally. The bacteria also produce an neurotoxic exotoxin called **tetanospasmin** (tetanus toxin) that travels by retrograde axonal transport through the lower motor neurons to the central nervous system. Here, it acts at the level of the anterior horn cells, **blocking inhibitory neurotransmission**, which results in the clinical syndrome of **tetanus**. Manifestations include increased muscle tone (eg, opisthotonos, lockjaw), painful spasms, and autonomic instability.

In the United States, the **tetanus toxoid vaccine** (formaldehyde-inactivated tetanus toxin) is part of routine childhood vaccinations. This vaccine stimulates a **humoral antibody response** against tetanus toxoid that prevents the toxoid from causing neurological damage. Tetanus is very rare in those who have been vaccinated; almost all cases occur in unvaccinated individuals or those who have not received appropriate booster vaccines.

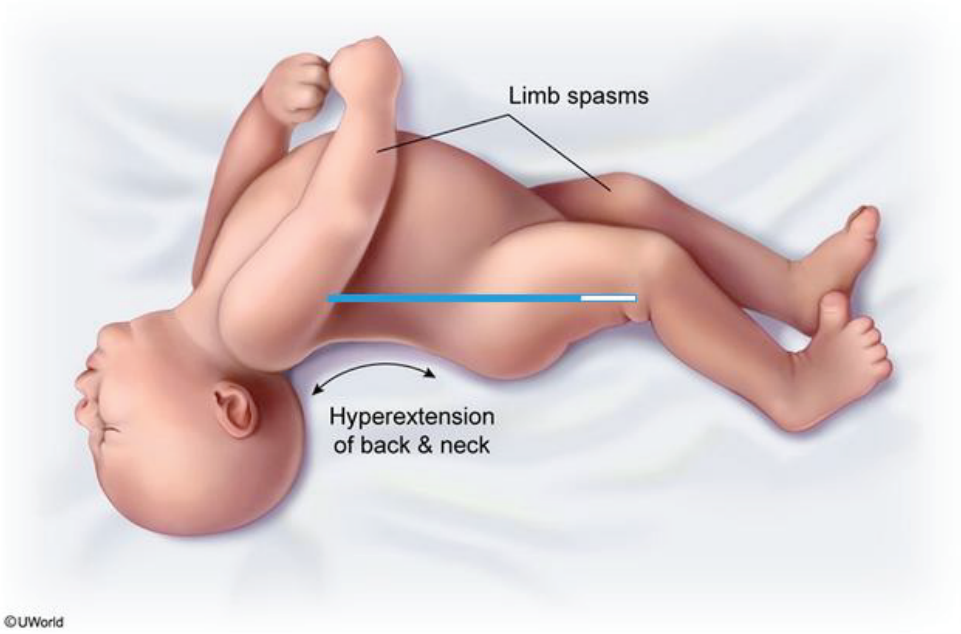
(Choice A) Activated macrophages engulf and digest foreign microbes and are the principal cell type responsible for granuloma formation. Although macrophages help clear bacteria locally from the wound

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Exhibit Display

Opisthotonos



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responsible for granuloma formation. Although macrophages help clear bacteria locally from the wound

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booster vaccines.

(Choice A) Activated macrophages engulf and digest foreign microbes and are the principal cell type responsible for granuloma formation. Although macrophages help clear bacteria locally from the wound, they would not be able to neutralize the tetanus toxin secreted by *Clostridium tetani*.

(Choice B) Circulating antibodies bind to extracellular pathogens and promote complement fixation and phagocytosis. Complement can opsonize and/or neutralize extracellular bacteria but would not impair the activity of tetanus toxin.

(Choice D) Neutrophils are responsible for phagocytosis of foreign organisms and are part of the initial response against extracellular pathogens. These cells play a role in nonspecific innate immunity but are not effective in eliminating the tetanus toxoid.

(Choice E) Cytotoxic CD8 lymphocytes play an important role in host defense against viral infections. They are also capable of destroying tumor cells and contribute to rejection reactions.

Educational objective:

Clostridium tetani produces the neurotoxin tetanospasmin, which blocks inhibitory neurotransmission in the spinal cord and leads to tonic muscular contraction. Tetanus is prevented by immunization with an inactivated toxoid that triggers the production of antitoxin antibodies (active immunity).

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A 45-year-old man comes to the office due to 3 months of night sweats, productive cough, decreased appetite, and a 5-kg (10-lb) weight loss. He travels frequently to Vietnam. Vital signs are normal. Examination reveals crackles in the right upper lobe of the lung. Chest x-ray reveals a right upper lobe infiltrate. Acid-fast bacilli are present on sputum smear. The patient is started on combination therapy with isoniazid, ethambutol, rifampin, pyrazinamide, and pyridoxine. One month later, he returns to the office reporting blurring of vision. Examination shows bilateral central scotomas. Which of the following is most likely responsible for this patient's visual symptoms?

A. Ethambutol
B. Isoniazid
C. Pyrazinamide
D. Pyridoxine
E. Rifampin

Submit

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- A. Ethambutol (75%)
- B. ~~Isoniazid~~ (11%)
- C. Pyrazinamide (5%)
- D. ~~Pyridoxine~~ (2%)
- E. ~~Rifampin~~ (4%)

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Drugs for treatment of tuberculosis		
Drug	**Mechanism of action**	**Side effects**
(R)ifampin	Inhibition of bacterial DNA-dependent RNA polymerase	GI side effects, rash, red-orange body fluids, cytopenias
(I)soniazid	Inhibition of mycolic acid synthesis	Neurotoxicity (give vitamin B_6/pyridoxine), hepatotoxicity
(P)yrazinamide	Unclear	Hepatotoxicity, hyperuricemia
(E)thambutol	Inhibition of arabinosyl transferase (?)	Optic neuropathy

GI = gastrointestinal.

This patient, who travels regularly to Vietnam and now has a cough, night sweats, and weight loss with a right upper lobe infiltrate on chest x-ray and acid-fast bacilli on sputum examination, likely has pulmonary

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This patient, who travels regularly to Vietnam and now has a cough, night sweats, and weight loss with a right upper lobe infiltrate on chest x-ray and acid-fast bacilli on sputum examination, likely has pulmonary **tuberculosis** (TB). Pulmonary TB is treated with a 4-drug regimen, sometimes referred to as RIPE: rifampin, isoniazid (INH), pyrazinamide, and ethambutol. The most notable side effect of **ethambutol** is **optic neuropathy**, which clinically manifests as decreased visual acuity, central scotoma, or color blindness. It may be reversible with discontinuation of the drug.

(Choices B and D) The most important side effect of INH is hepatotoxicity. INH is also associated with peripheral neuropathy, which is due to the drug's interference with pyridoxine metabolism and can be prevented by pyridoxine administration.

(Choice C) The most important side effects of pyrazinamide are hepatotoxicity and hyperuricemia (can exacerbate gout).

(Choice E) Rifampin can cause body fluids (eg, urine, tears) to turn red. This condition is benign.

Educational objective:
Ethambutol can cause optic neuropathy that results in color blindness, central scotoma, and decreased visual acuity. This adverse side effect may be reversed with discontinuation of the drug.

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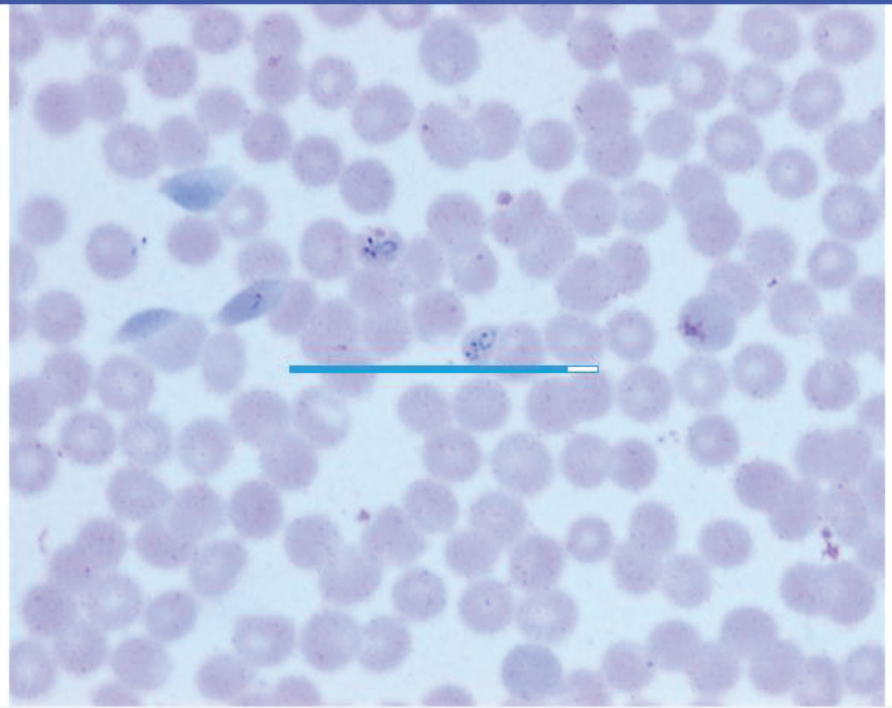
A 65-year-old man comes to the emergency department with fevers and malaise over the last 48 hours. He initially experienced fevers and chills, which subsequently progressed to fatigue to the point that he had difficulty performing routine tasks this morning. He has also had a mild headache. The patient lives in eastern Massachusetts with his wife. He is retired and spends time gardening and swimming at a local public pool. He traveled to Thailand 2 years ago with his family and to Florida 2 months ago. His temperature is 38.9 C (102 F), blood pressure is 122/70 mm Hg, and pulse is 114/min and regular. The oropharynx is dry without lesions. Lung examination reveals coarse crackles bilaterally. The patient's abdomen is soft and mildly tender throughout with palpable splenomegaly. He has no rash or open wounds. A peripheral blood smear (as shown in the exhibit) is performed. What is the most likely source of this infection?

A. *Aedes* mosquito
B. Brown recluse spider
C. Dog bite
D. Freshwater consumption
E. *Ixodes* tick

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E. Ixodes tick

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A. *Aedes* mosquito
B. Brown recluse spider
C. Dog bite
D. Freshwater consumption
E. *Ixodes* tick
F. Scratch from a garden bush
G. Spore inhalation

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temperature is 38.9 C (102 F), blood pressure is 122/70 mm Hg, and pulse is 114/min and regular. The oropharynx is dry without lesions. Lung examination reveals coarse crackles bilaterally. The patient's abdomen is soft and mildly tender throughout with palpable splenomegaly. He has no rash or open wounds. A peripheral blood smear (as shown in the exhibit) is performed. What is the most likely source of this infection?

- A. *Aedes* mosquito (34%)
- B. Brown recluse spider (0%)
- C. Dog bite (0%)
- D. Freshwater consumption (6%)
- ✓ E. *Ixodes* tick (47%)
- F. Scratch from a garden bush (5%)
- G. Spore inhalation (5%)

Correct

47%

01 min, 52 secs

01/24/2021

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Babesiosis	
Epidemiology	• Agent: *Babesia microti* • Vector: *Ixodes scapularis* **tick** (same for Lyme disease & HGA) • Geographic distribution: Northeastern United States
Clinical manifestations	• Signs & symptoms: Fevers, fatigue, myalgias, headache, **flulike symptoms** (if **severe**: ARDS, CHF, DIC, splenic rupture) • Laboratory studies: **Anemia, thrombocytopenia**, ↑LFTs
Diagnosis	• Thin blood smear (Wright/Giemsa stains): **Intraerythrocytic** pleomorphic **ring forms** (occasional "Maltese crosses")

ARDS = acute respiratory distress syndrome; **CHF** = congestive heart failure; **DIC** = disseminated intravascular coagulation; **HGA** = human granulocytic anaplasmosis; **LFTs** = liver function tests.

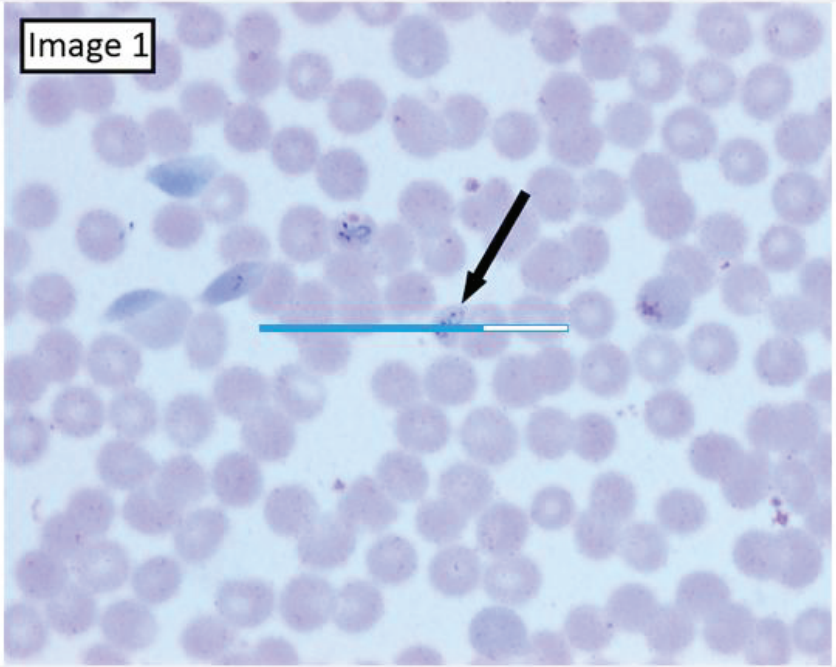
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This patient with an acute febrile illness has a peripheral blood smear showing intraerythrocytic ring inclusions. Parasites that can potentially cause disease in red blood cells include *Plasmodium* (malaria) and *Babesia* (babesiosis). In this patient, the epidemiology - residence in **northeastern United States**, outdoor exposure in the summer - is suggestive of **babesiosis**. This organism is transmitted by the *Ixodes scapularis* tick, which is also a vector for *Borrelia burgdorferi*, the bacteria that cause Lyme disease.

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Babesiosis Babesiosis: Babesia microti



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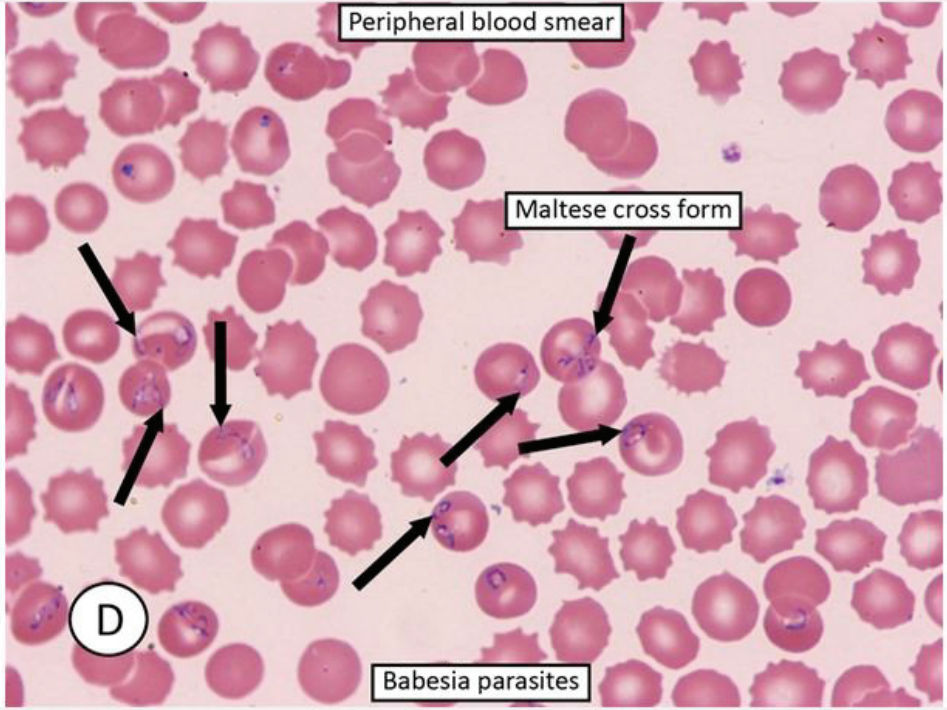
scapularis tick, which is also a vector for *Borrelia burgdorferi*, the bacteria that cause Lyme disease.

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Exhibit Display

Babesiosis Babesiosis: Babesia microti



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and *Babesia* (babesiosis). In this patient, the epidemiology - residence in **northeastern United States**, outdoor exposure in the summer - is suggestive of **babesiosis**. This organism is transmitted by the *Ixodes scapularis* tick, which is also a vector for *Borrelia burgdorferi*, the bacteria that cause Lyme disease.

(Choice A) *Aedes* is the vector for dengue fever and chikungunya, which have been diagnosed in Florida but have different presentations (eg, rash, arthralgias) and a short incubation period (<14 days). Malaria is transmitted by *Anopheles* and is endemic in Thailand; although it can also cause intraerythrocytic ring inclusions, it has a typical incubation period of weeks (this patient visited Thailand years ago).

(Choice B) Brown recluse spider bites can cause fever and malaise and less commonly anemia; however, they would not be associated with intraerythrocytic organisms.

(Choice C) Dog bites can be associated with a variety of organisms causing soft-tissue infection, including *Pasteurella*, streptococci, and staphylococci.

(Choice D) Freshwater consumption can be associated with intraintestinal bacterial and parasitic infections such as cryptosporidiosis and giardiasis. However, these infections typically cause gastrointestinal illnesses.

(Choice F) Exposure to plants and soil can be associated with bacterial infections, including *Nocardia* and fungal infections such as sporotrichosis. These most commonly present as soft-tissue infections; systemic

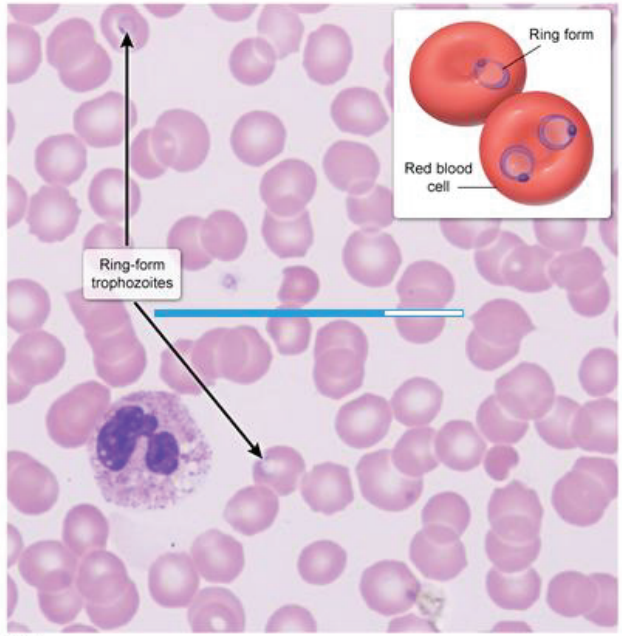
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and *Babesia* (babesiosis). In this patient, the epidemiology, residence in **northeastern United States**

Exhibit Display

Plasmodium



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fungal infections such as sporotrichosis. These most commonly present as soft-tissue infections; systemic

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(Choice D) Freshwater consumption can be associated with intraintestinal bacterial and parasitic infections such as cryptosporidiosis and giardiasis. However, these infections typically cause gastrointestinal illnesses.

(Choice F) Exposure to plants and soil can be associated with bacterial infections, including *Nocardia* and fungal infections such as sporotrichosis. These most commonly present as soft-tissue infections; systemic infections are rare in immunocompetent patients.

(Choice G) Fungal spore inhalation can lead to pulmonary infections, including histoplasmosis and blastomycosis. These organisms are not endemic to the northeastern United States and are not associated with intraerythrocytic organisms.

Educational objective:
Babesiosis should be considered in patients with febrile illness who reside in geographic areas where they are exposed to *Ixodes* ticks. Diagnosis can be established with the identification of intraerythrocytic organisms on peripheral blood smear.

References

- Babesiosis.
- Human babesiosis.

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A 1-year-old boy is brought to the emergency department by his mother because of high fever, irritability, and photophobia. He recently underwent ventriculoperitoneal shunt placement for congenital hydrocephalus. On physical examination, his temperature is 38.3° C (101° F), and passive flexion of the neck results in spontaneous flexion of the hips and knees. Blood cultures grow coagulase-negative *Staphylococcus*. Which of the following is the most important virulence mechanism by which this bacterium causes disease?

A. Intracellular existence
B. Outer polysaccharide capsule
C. Presence of protein A on the cell wall
D. Release of exotoxins
E. Synthesis of an extracellular polysaccharide matrix

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A 1-year-old boy is brought to the emergency department by his mother because of high fever, irritability, and photophobia. He recently underwent ventriculoperitoneal shunt placement for congenital hydrocephalus. On physical examination, his temperature is 38.3° C (101° F), and passive flexion of the neck results in spontaneous flexion of the hips and knees. Blood cultures grow coagulase-negative *Staphylococcus*. Which of the following is the most important virulence mechanism by which this bacterium causes disease?

A. ~~Intracellular existence~~ (1%)

B. ~~Outer polysaccharide capsule~~ (15%)

C. Presence of protein A on the cell wall (27%)

D. ~~Release of exotoxins~~ (13%)

✓ E. Synthesis of an extracellular polysaccharide matrix (42%)

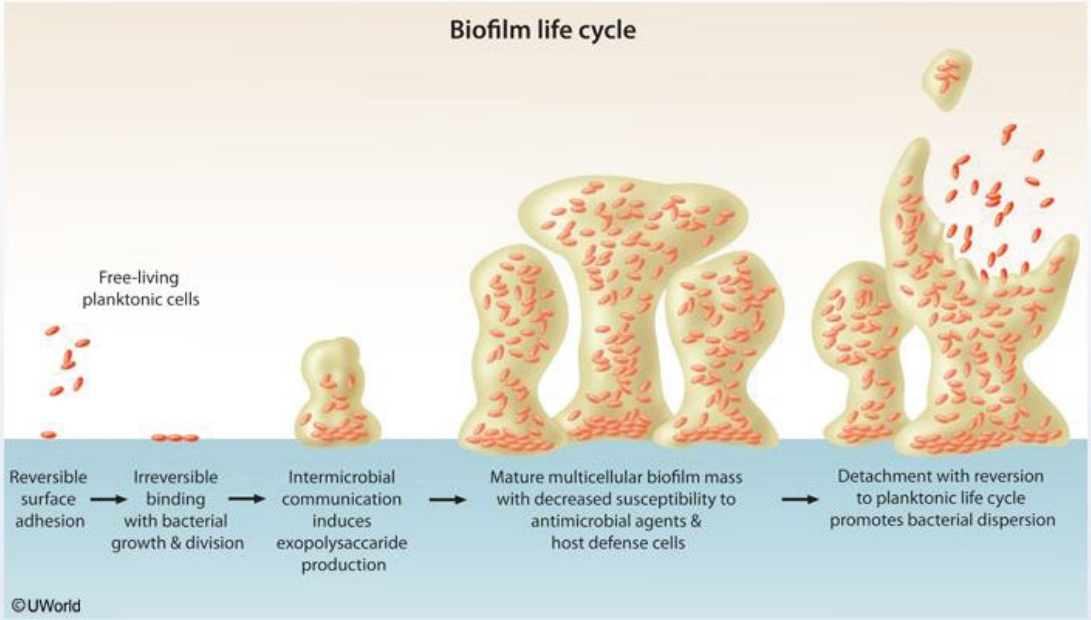
Correct

42%
Answered correctly

02 mins, 03 secs
Time Spent

01/11/2021
Last Updated

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Staphylococcus epidermidis, a coagulase-negative *Staphylococcus* species and a component of normal skin flora, is one of the most common causes of infections associated with foreign bodies (including ventriculoperitoneal shunts). *S epidermidis* is adept at causing foreign body infections because of its ability to form biofilms.

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Once introduced into the body, foreign bodies quickly become coated with a layer of host proteins, including fibrinogen and fibronectin. These proteins then serve as binding sites for *S epidermidis*. After attachment occurs, the bacteria multiply and communicate with one another to induce synthesis of an extracellular polysaccharide matrix that encases the bacteria. The resulting biofilm functions as a barrier to antibiotic penetration and interferes with host defenses, including opsonization, neutrophil migration, and even T lymphocyte activation. Once mature, these biofilms can disperse individual pathogen "seeds" (planktonic cells) into the bloodstream and surrounding areas, further disseminating the infection. Definitive treatment of infections caused by biofilm-producing organisms often requires removal of the foreign body.

(Choice A) *S epidermidis* is not an intracellular organism. Examples of obligate intracellular organisms include *Chlamydiae* and *Rickettsiae*. Facultative intracellular organisms include *Legionella*, *Listeria*, *Mycobacterium*, *Neisseria*, and *Salmonella*.

(Choice B) *S epidermidis* is not an encapsulated bacterium. Examples of encapsulated bacteria are *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, and *Neisseria meningitidis*. Asplenic individuals are unable to opsonize encapsulated pathogens and are at risk of infection from these organisms.

(Choice C) Protein A is a surface protein found on the cell wall of *Staphylococcus aureus* that binds to the

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Biofilm-producing organism	Common settings
Staphylococcus epidermidis	Prosthetic devices, intravenous catheters
Streptococcus mutans & *Streptococcus sanguinis*	Dental plaques
Pseudomonas aeruginosa	Cystic fibrosis pneumonia, contact lenses
Viridans group streptococci	Endocarditis
Nontypable *Hemophilus influenza*	Otitis media

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(Choice C) Protein A is a surface protein found on the cell wall of *Staphylococcus aureus* that binds to the

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(Choice C) Protein A is a surface protein found on the cell wall of *Staphylococcus aureus* that binds to the Fc region of immunoglobulins. *S aureus* uses Protein A to inhibit opsonization and phagocytic engulfment.

(Choice D) Exotoxin production is not a known pathogenic mechanism of *S epidermidis*. Examples of well- known exotoxins include staphylococcal enterotoxins (food poisoning), botulinum toxin, diphtheria toxin, tetanus toxin, and pertussis toxin.

Educational objective:

Staphylococcus epidermidis is a common cause of foreign body infections due to its ability to produce adherent biofilms.

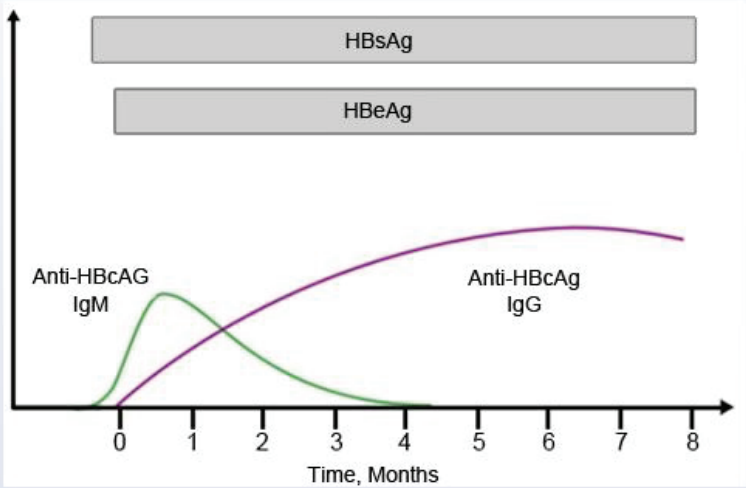
References

- Biofilms: microbes and disease.

Microbiology Infectious Diseases Staphylococci

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A 25-year-old man is hospitalized with fever, anorexia, and fatigue. He admits to IV drug abuse and many episodes of unprotected sex over the past few years. His condition is treated and he is discharged from the hospital. The patient follows up with his physician regularly over the next 8 months, and the following serologic marker dynamics are obtained (see the graph below).

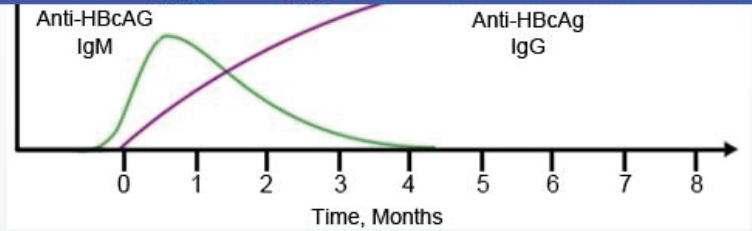


*Grey bars indicate the detectable presence of the specified serum marker.

This patient most likely:

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*Grey bars indicate the detectable presence of the specified serum marker.

This patient most likely:

A. Had acute hepatitis B and has successfully recovered

B. Had an exacerbation of preexisting hepatitis B

C. Had acute hepatitis B that has progressed to chronic hepatitis with low infectivity

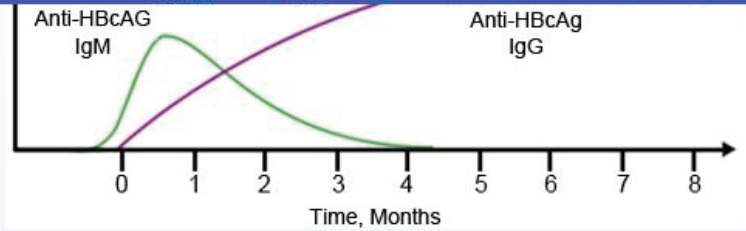
D. Had acute hepatitis B that has progressed to chronic hepatitis with high infectivity

E. Was vaccinated against HBV during the hospitalization

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*Grey bars indicate the detectable presence of the specified serum marker.

This patient most likely:

A. ~~Had acute hepatitis B and has successfully recovered~~ (5%)

B. ~~Had an exacerbation of preexisting hepatitis B~~ (1%)

C. Had acute hepatitis B that has progressed to chronic hepatitis with low infectivity (7%)

D. Had acute hepatitis B that has progressed to chronic hepatitis with high infectivity (83%)

E. Was vaccinated against HBV during the hospitalization (1%)

Correct

83%

01 min, 08 secs

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The serologic markers for hepatitis B infection appear on a predictable timeline with a long asymptomatic incubation period (lasting an average of 6-8 weeks) followed by acute disease lasting several weeks to months. HBsAg first appears before the onset of symptoms, peaks when the patient is most ill, and then becomes undetectable in 3-6 months (unless the disease progresses to a chronic phase). Shortly after HBsAg first appears, HBeAg and HBV DNA can be detected in the serum and are markers of active viral replication. Anti-HBcAg IgM and elevated serum transaminases appear shortly before symptom onset. Over the next few months, the anti-HBcAg IgM component is replaced with an IgG component. Anti-HBeAg appears shortly after HBeAg vanishes and suggests subsiding viral activity (transition from high viral replication/infectivity to low viral replication/infectivity). Anti-HBsAg IgG arises once the acute disease has resolved (unless the disease progresses to a chronic phase), and is typically not detectable until weeks or months after HBsAg has disappeared. This antibody may persist indefinitely, conferring lifelong immunity.

Given this serologic marker graph, it appears that this patient has a persistence of HBsAg and HBeAg over a long period with low to moderate levels of anti-HBcAg IgG and no detectable Anti-HBsAg. These findings are suggestive of an acute hepatitis B infection that has not resolved, but rather has progressed to a highly infectious chronic hepatitis B (note the persistence of HBeAg and lack of anti-HBeAg).

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(Choice A) Were this patient to have fully recovered from his bout of acute hepatitis B, all antigens should have dropped to undetectable levels and he should have high levels of anti-HBsAg IgG and anti-HBcAg IgG.

(Choice B) An exacerbation of preexisting hepatitis B would be characterized by a decline followed by a spike in antigen levels.

(Choice C) Acute hepatitis B that progressed to chronic hepatitis with low infectivity would be indicated by a graph similar to the one shown for this patient. However, there would be low or undetectable levels of HBeAg (the marker for high infectivity) and likely detectable quantities of anti-HBeAg.

(Choice E) Vaccination against HBV would be identified by a surge in anti-HBsAb with no anti-HBcAg, anti-HBeAg, or viral antigens detected.

Educational objective:
If HBeAg persists for several months and host anti-HBeAg remain at low or undetectable levels, suspect chronic hepatitis B infection with high infectivity.

Microbiology	Infectious Diseases	Hepatitis b
Subject	System	Topic

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A 64-year-old man comes to the office due to several days of low-grade fever and productive cough. He has smoked a pack of cigarettes daily for 30 years and has been hospitalized several times for respiratory infections. Temperature is 37.2 C (99 F), blood pressure is 130/70 mm Hg, pulse is 82/min, and respirations are 14/min. Pulse oximetry shows 98% on ambient air. Lung auscultation reveals rhonchi that clear with coughing. Sputum cultures in specialized media grow round-to-oval, budding yeast, which form germ tubes when incubated at 37 C in serum. Which of the following best explains the presence of the organism in this patient's sputum sample?

A. Colonization of a preexisting lung cavity
B. Contamination by normal oral flora
C. Embolization of infectious microthrombi
D. Lung infection from inhaled microconidia
E. Proliferation of previously latent organism

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A. Colonization of a preexisting lung cavity (14%)
B. Contamination by normal oral flora (54%)
C. ~~Embolization of infectious microthrombi~~ (1%)
D. ~~Lung infection from inhaled microconidia~~ (24%)
E. ~~Proliferation of previously latent organism~~ (5%)

54%
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02/23/2021

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This patient's 30-pack-year smoking history, low-grade fever, productive cough, normal pulse oximetry, and pulmonary rhonchi suggest a chronic obstructive pulmonary disease **(COPD) exacerbation**. Although expectorated sputum cultures are not routinely obtained in patients with COPD exacerbation, they may help identify the underlying respiratory pathogen in certain cases (eg, concern for drug-resistant organism). However, positive expectorated sputum results often indicate contamination with oral flora rather than true infection.

This patient's sputum culture grew ***Candida albicans***, an oval, budding yeast that forms true hyphae (**"germ tubes"**) when incubated at body temperature (37 C). *C albicans* is a **normal commensal** of the skin and gastrointestinal tract that occasionally causes mucocutaneous infection (eg, vulvovaginitis, cutaneous candidiasis) but **rarely causes invasive disease** (eg, sepsis, chorioretinitis, endocarditis); invasive infection primarily occurs in those with significant neutropenia or indwelling vascular catheters (which provide a portal of entry from the skin into the bloodstream). Therefore, the presence of *C albicans* on a sputum sample almost always indicates **contamination with oral flora** rather than true infection.

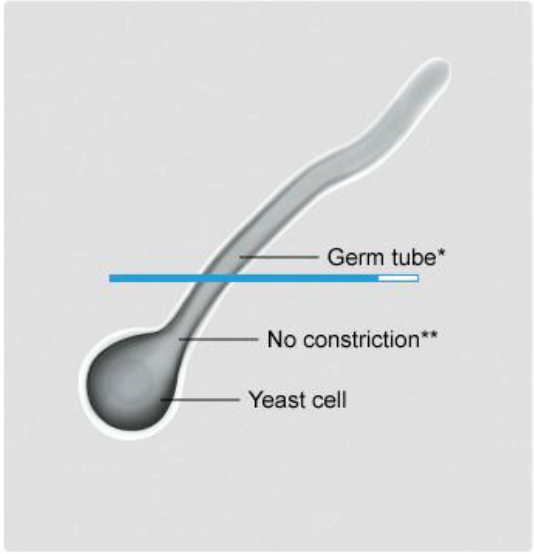
Other common oral contaminants (that almost never indicate true infection) include coagulase-negative staphylococci and enterococci.

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Candida albicans



*Hypha formed when incubated in serum at 37°C
**In contrast to pseudohyphae

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(Choice A) *Aspergillus fumigatus*, a fungus with dichotomous, branching hyphae, can colonize preexisting lung cavities, thereby creating a "fungus ball" (aspergilloma). Most aspergillomas are asymptomatic, and the organism does not resemble a yeast in culture.

(Choice C) *Candida* infective endocarditis can cause pulmonary infection due to septic pulmonary emboli. However, this condition is rare and is typically seen in patients with indwelling vascular catheters or history of intravenous drug use.

(Choice D) *Histoplasma capsulatum* is a dimorphic fungus that is inhaled as microconidia and converts to a small, ovoid yeast in the lungs. It replicates by forming narrow-based buds, not germ tubes. In addition, most clinically significant cases are associated with pneumonia, not bronchitis.

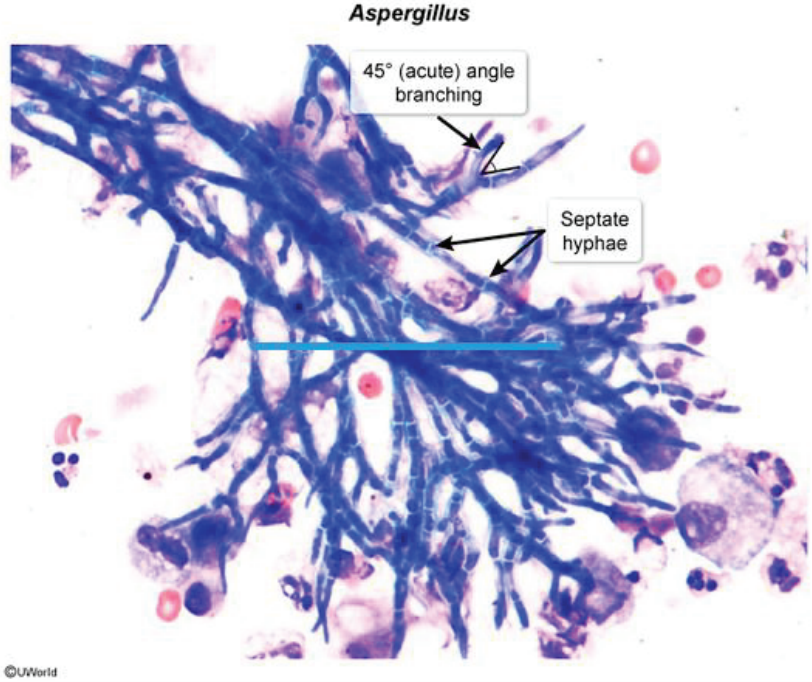
(Choice E) *Mycobacterium tuberculosis* pulmonary infection is usually marked by months or years of asymptomatic latency (within granulomas) that may later reactivate and cause cavitary lung disease. Sputum culture would reveal acid-fast bacilli, not yeast.

Educational objective:
Expectorated sputum cultures are often contaminated by normal oral flora. The growth of *Candida albicans*, a normal commensal of the gastrointestinal tract and skin, almost always indicates oral contamination rather than true pulmonary infection.

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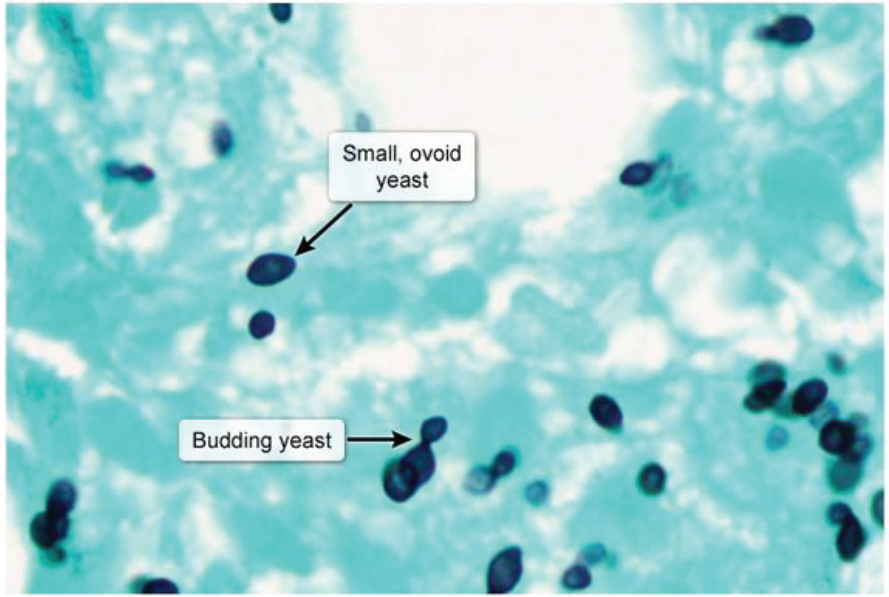
contamination rather than true pulmonary infection

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Histoplasma



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Methenamine silver stain

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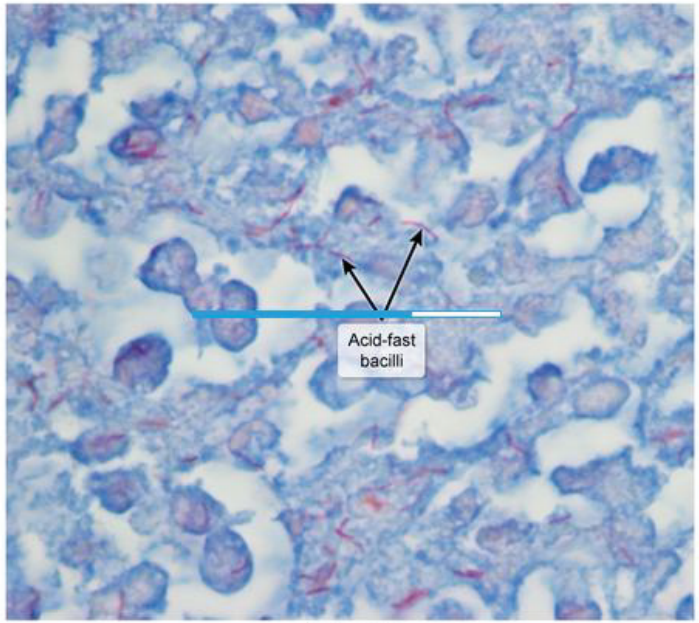
contamination rather than true pulmonary infection

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Exhibit Display

Mycobacteria



Acid-fast stain

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contamination rather than true pulmonary infection

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Educational objective:
Expectorated sputum cultures are often contaminated by normal oral flora. The growth of *Candida albicans*, a normal commensal of the gastrointestinal tract and skin, almost always indicates oral contamination rather than true pulmonary infection.

Microbiology Infectious Diseases Normal flora

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A 42-year-old man comes to the office due to 2 weeks of progressive fever, chills, abdominal discomfort, and loose stools, which began during a trip to Southeast Asia. He received no pre-travel vaccinations and did not strictly follow food and water safety precautions during the trip. The patient has no chronic medical conditions but has experienced a prior episode of *Salmonella enteritidis* gastroenteritis, which resolved with symptomatic care. Temperature is 39.4 C (103 F), blood pressure is 110/64 mm Hg, pulse is 62/min, and respirations are 18/min. Physical examination reveals a faint macular rash on the trunk. There is mild tenderness on palpation of lower abdominal quadrants with no guarding or rebound tenderness. Blood culture grows non-lactose fermenting gram-negative rods. Which of the following best explains the prolonged and severe disease course from this pathogen compared to the patient's previous bacterial infection?

A. Contact-dependent host cytotoxicity
B. Cross-reacting antibody formation
C. Extensive intra-phagocytic multiplication
D. Potent exotoxin production
E. Villus epithelial cell destruction

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A. Contact-dependent host cytotoxicity (6%)
B. Cross-reacting antibody formation (12%)
C. Extensive intra-phagocytic multiplication (34%)
D. Potent exotoxin production (26%)
E. Villus epithelial cell destruction (19%)

Correct

34%

02 mins, 54 secs

03/24/2021

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	Nontyphoidal *Salmonella*	Typhoidal *Salmonella*
Epidemiology	• *S enterica* • **Poultry/eggs**, exotic pets • **Foodborne** (primarily) • Industrialized countries	• *S typhi*, *S paratyphi* • Humans only • Water/food contamination • **Developing countries**
Pathophysiology	Invasion of enterocytes → massive neutrophil-mediated inflammatory response in lamina propria/Peyer's patches → control of infection (usually)	Invasion of enterocytes → blunted neutrophil response due to **capsular antigen Vi** → extensive intracellular replication in macrophages → spread through lymphatics and RES
Manifestations	**Gastroenteritis** • Self-limited watery diarrhea • Rarely invasive (<5%): osteomyelitis, mycotic aneurysm, endocarditis	**Typhoid fever** • Progressive fever (pulse-temperature dissociation) • Rose spots, abdominal pain • HSM, GI bleed, perforation

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Salmonella are gram-negative, non-lactose–fermenting, motile enteric rods that are divided into nontyphoidal (eg, *S enteritidis*) and typhoidal (eg, *S typhi*, *S paratyphi*) strains. Both strains are able to cause disease by penetrating enterocytes, where they then travel in vacuoles from the apical to the basolateral end of the cell to invade the lamina propria. However, the pathogenesis then diverges, as follows:

- **Nontyphoidal species** are phagocytosed by neutrophils and macrophages in the lamina propria and induce a massive inflammatory response marked by dramatic neutrophil infiltration. The cytokine-mediated inflammatory response typically results in 1-5 days of **gastroenteritis** (eg, watery diarrhea, abdominal pain, and fever). Most cases resolve without intervention.
- In contrast, **typhoidal species** contain a specialized **capsular antigen** called **Vi** (short for virulence) that inhibits neutrophil recruitment and phagocytosis. This limits the acute inflammatory response that helps contain the nontyphoidal species. It also inhibits macrophages from generating an oxidative burst to destroy the bacteria, which allows the pathogen to undergo extensive **unchecked intracellular replication** and subsequently disseminate through the lymphatic and reticuloendothelial system. This results in **typhoid fever**.

Typhoidal strains of *Salmonella* are found only in humans and are typically transmitted by the consumption

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system. This results in **typhoid fever**.

Typhoidal strains of *Salmonella* are found only in humans and are typically transmitted by the consumption of food or water contaminated by human feces. Typhoid *Salmonella* is endemic to areas where sanitation is poor. Travelers may become ill if they are unvaccinated (typhoid vaccine) and do not strictly adhere to food and water safety precautions. Manifestations begin approximately a week after transmission with an **escalating fever** that is often associated with relative bradycardia (**pulse-temperature dissociation**). Approximately a week later, patients typically develop abdominal pain, diarrhea or constipation, and transient salmon-colored macules (**rose spots**) on the trunk. Serious complications such as intestinal bleeding and perforation can occur later.

(Choice A) Contact between *Entamoeba histolytica* and the host cell results in the insertion of an amebic channel-forming protein in the host cell membrane that causes cell death. Manifestations of *E histolytica* infection typically include bloody diarrhea (colitis) and/or extraintestinal manifestations (eg, liver abscess).

(Choice B) *Campylobacter* infection is a common cause of self-limited acute infectious diarrhea and may result in the formation of cross-reacting antibodies to GM1 ganglioside, leading to Guillain-Barré syndrome. *Campylobacter* symptoms usually last <7 days and do not include rose spots or temperature dissociation.

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result in the formation of cross-reacting antibodies to GM1 ganglioside, leading to Guillain-Barré syndrome. *Campylobacter* symptoms usually last <7 days and do not include rose spots or temperature dissociation.

(Choice D) *Shigella* and enterohemorrhagic *Escherichia coli* produce a potent exotoxin that can result in cell death, hemorrhagic colitis, and systemic manifestations (eg, hemolytic-uremic syndrome). Exotoxins do not play a prominent role in *Salmonella* infection.

(Choice E) Rotavirus and *giardia* damage intestinal villi, which leads to intestinal malabsorption due to villous blunting and decreased levels of brush border enzymes (eg, maltase, sucrase, lactase).

Educational objective:
Typhoid strains of *Salmonella* contain a capsular antigen (Vi) that inhibits neutrophil phagocytosis, neutrophil recruitment, and macrophage-mediated destruction. Therefore, typhoid strains are able to undergo extensive replication within the intracellular space of macrophages with subsequent spread through the lymphatic and reticuloendothelial system, leading to a widespread systemic disease (typhoid fever).

Microbiology	Infectious Diseases	Typhoid
Subject	System	Topic

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A 65-year-old man is brought to the emergency department due to high fevers and confusion. His family says that for the past couple of days, he has been acting strangely and has been disoriented. He has also had severe headaches. This morning he was difficult to arouse and reportedly had a seizure on the way to the hospital. His temperature is 39.4 C (103 F), blood pressure is 140/90 mm Hg, and pulse is 112/min. The patient is obtunded with preserved brainstem reflexes and reduced motor responses to pain. CT scan of the head without contrast is negative. Cerebrospinal fluid analysis reveals an elevated opening pressure with a hemorrhagic lymphocytic pleocytosis, increased protein, and normal glucose. An MRI of the brain reveals an abnormal signal in the bilateral temporal lobes. A drug that inhibits which of the following would be most effective in treating this patient's condition?

A. Bacterial cell wall synthesis
B. Bacterial folic acid metabolism
C. Bacterial nucleic acid synthesis
D. Bacterial ribosomes
E. Viral DNA polymerase

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A. Bacterial cell wall synthesis
B. Bacterial folic acid metabolism
C. Bacterial nucleic acid synthesis
D. Bacterial ribosomes
E. Viral DNA polymerase
F. Viral protease
G. Viral reverse transcriptase
H. Viral RNase H

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of the head without contrast is negative. Cerebrospinal fluid analysis reveals an elevated opening pressure with a hemorrhagic lymphocytic pleocytosis, increased protein, and normal glucose. An MRI of the brain reveals an abnormal signal in the bilateral temporal lobes. A drug that inhibits which of the following would be most effective in treating this patient's condition?

A. Bacterial cell wall synthesis (3%)
B. Bacterial folic acid metabolism (1%)
C. Bacterial nucleic acid synthesis (2%)
D. Bacterial ribosomes (1%)
✓ E. Viral DNA polymerase (75%)
F. Viral protease (8%)
G. Viral reverse transcriptase (5%)
H. Viral RNase H (2%)

75%
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This patient has **herpes simplex virus (HSV) encephalitis**, which can cause acute/subacute changes in mental status, seizures, headache, and, in some cases, focal neurologic deficits. Cerebrospinal fluid (CSF) analysis usually reveals a **hemorrhagic lymphocytic pleocytosis** with **increased** protein and normal glucose. On neuroimaging, the classic finding includes the presence of an abnormal MRI signal in the bilateral **temporal lobes**. The treatment for HSV encephalitis is intravenous **acyclovir**, a nucleoside analog that, once activated, competes with deoxyguanosine triphosphate for **viral DNA polymerase**; when acyclovir triphosphate becomes incorporated into the replicating viral DNA chain, viral DNA synthesis is terminated.

Viral proteases are responsible for cleavage of protein precursors necessary for the production of infectious viral particles. Protease inhibitors are important in the treatment of HIV and hepatitis C **(Choice F).** Viral RNase H (removes the RNA primer, allowing for completion of newly synthesized DNA) and viral reverse transcriptase (generates complementary DNA from an RNA template) are important pharmaceutical targets for the treatment of retroviruses such as HIV **(Choices G and H).**

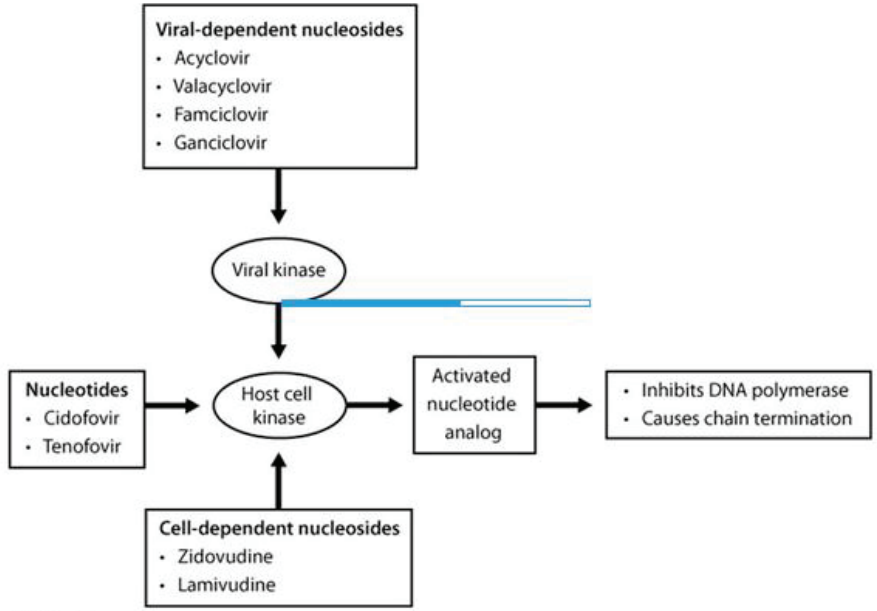
(Choices A, B, C, and D) Bacterial meningitis can present similarly to HSV encephalitis; however, unlike HSV encephalitis, CSF analysis typically shows a nonhemorrhagic neutrophilic pleocytosis with low glucose and elevated protein and there is no predilection for the temporal lobes.

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Exhibit Display

Activation of nucleoside analog drugs



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glucose and elevated protein and there is no predilection for the temporal lobes.

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viral particles. Protease inhibitors are important in the treatment of HIV and hepatitis C **(Choice F).** Viral RNase H (removes the RNA primer, allowing for completion of newly synthesized DNA) and viral reverse transcriptase (generates complementary DNA from an RNA template) are important pharmaceutical targets for the treatment of retroviruses such as HIV **(Choices G and H).**

(Choices A, B, C, and D) Bacterial meningitis can present similarly to HSV encephalitis; however, unlike HSV encephalitis, CSF analysis typically shows a nonhemorrhagic neutrophilic pleocytosis with low glucose and elevated protein and there is no predilection for the temporal lobes.

Educational objective:

The most effective treatment for herpes simplex virus encephalitis is intravenous acyclovir; whose mechanism of action is complete inhibition of the viral DNA polymerase (synthesizes viral DNA).

References

- Herpes simplex encephalitis: from virus to therapy.

Microbiology	Infectious Diseases	Acyclovir
Subject	System	Topic

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A 34-year-old man comes to the emergency department due to 2 days of fever, malaise, and myalgia. He has also had worsening shortness of breath and cough. The patient works in the mail room at a large company, does not smoke cigarettes, and drinks alcohol occasionally. Chest imaging shows lung infiltrates and prominent widening of the mediastinum. Sputum and blood cultures yield large, gram-positive rods that form colonies resembling a "Medusa head." Which of the following is the most likely bacterial virulence factor contributing to this patient's condition?

A. Antiphagocytic D-glutamate capsule
B. Antiphagocytic polysaccharide capsule
C. IgG-binding, outer membrane protein
D. Intracellular polyphosphate granules
E. Peritrichous flagella

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A. Antiphagocytic D-glutamate capsule (67%)
B. Antiphagocytic polysaccharide capsule (15%)
C. IgG-binding, outer membrane protein (4%)
D. Intracellular polyphosphate granules (6%)
E. Peritrichous flagella (6%)

Correct

67%
Answered correctly

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Bacillus anthracis is a large, nonmotile, nonhemolytic, gram-positive rod that forms colonies in culture with multiple curled extensions at the edges that resemble a "**Medusa head**." Because the organism proliferates in soil contaminated with manure, pasture-grazing herbivores such as sheep, cattle, and horses are at greatest risk for infection. However, transmission to humans occasionally occurs when *B anthracis* **spores** are inhaled, ingested, or inoculated into the skin.

Inhalation of spores into the alveoli causes **pulmonary anthrax**. Alveolar macrophages phagocytose the spores and bring them to mediastinal lymph nodes, where the spores germinate into vegetative rods and multiply. The vegetative form of the bacteria contains a **polypeptide capsule** composed of **D-glutamic acid**, which is antiphagocytic. *B anthracis* rods also produce a potent **exotoxin complex** composed of edema factor, lethal factor, and protective antigen, which enter host cells and cause cell death.

Initial manifestations of infection are nonspecific (eg, myalgia, fever, malaise), but proliferation of the bacteria in the mediastinum eventually causes **hemorrhagic mediastinitis** (often visible on chest x-ray as a widened mediastinum). Subsequent dissemination through the bloodstream causes shock, brain edema/hemorrhage, and death. Although pulmonary anthrax is quite rare, it can be seen in individuals who handle contaminated hides or animal hair ("woolsorter's disease") or those exposed to aerosolized **biologic weapons** (eg, opening contaminated mail).

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(Choice B) Many bacteria (eg, *Streptococcus pneumoniae*) are resistant to phagocytosis due to the presence of a polysaccharide capsule. However, *B anthracis* has a polypeptide, not polysaccharide, capsule.

(Choice C) *Staphylococcus aureus* produces protein A, which binds the Fc portion of IgG. This inhibits opsonization and complement-mediated killing of the bacteria.

(Choice D) Intracellular polyphosphate granules are characteristic of *Corynebacterium diphtheriae*; they can be visualized on microscopy after growing the pathogen on Loeffler medium and staining it with methylene blue.

(Choice E) Peritrichous flagella (flagella distributed uniformly over the entire surface of a bacterial cell) are not present on the surface of *B anthracis* as this organism is nonmotile. Peritrichous flagella are characteristic of highly motile organisms such as *Proteus mirabilis*.

Educational objective:
Bacillus anthracis is a large, sporulating, gram-positive rod that is encased in an antiphagocytic polypeptide capsule composed of D-glutamic acid. Inhalation of *B anthracis* spores can cause pulmonary anthrax, which is usually characterized by nonspecific symptoms followed by hemorrhagic mediastinitis, shock, and death.

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A 42-year-old man with HIV comes to the emergency department with 3 days of abdominal pain, decreased appetite, and diarrhea. Temperature is 38 C (100.4 F), blood pressure is 98/60 mm Hg, and pulse is 110/min. Abdominal examination shows tenderness over the left lower quadrant without guarding or rebound tenderness. CD4 count is 38/mm^3. Colonoscopy shows erythematous, friable mucosa with superficial ulcerations in the sigmoid and descending colon. Biopsy from the ulcers reveals inflammatory infiltrate, mucosal necrosis, and enlarged endothelial cells with large, ovoid nuclei containing prominent basophilic deposits.

Item 1 of 2

Which of the following is the most likely cause of this patient's gastrointestinal symptoms?

A. Disseminated mycobacterial infection
B. Infection by a modified acid-fast protozoan
C. Mucosal invasion by a commensal yeast
D. Reactivation of a herpesvirus

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Item 1 of 2

Which of the following is the most likely cause of this patient's gastrointestinal symptoms?

A. Disseminated mycobacterial infection
B. Infection by a modified acid-fast protozoan
C. Mucosal invasion by a commensal yeast
D. Reactivation of a herpesvirus
E. Toxin from an anaerobic bacteria

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Item 1 of 2

Which of the following is the most likely cause of this patient's gastrointestinal symptoms?

A. ~~Disseminated mycobacterial infection~~ (7%)
B. ~~Infection by a modified acid-fast protozoan~~ (32%)
C. ~~Mucosal invasion by a commensal yeast~~ (10%)
D. Reactivation of a herpesvirus (37%)
E. ~~Toxin from an anaerobic bacteria~~ (10%)

Correct

37%
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Common opportunistic causes of diarrhea in HIV patients

Pathogen	Histopathologic findings
Cytomegalovirus	• Multiple ulcers & mucosal erosions • Large cells with basophilic intranuclear & intracytoplasmic inclusions
Cryptosporidium	• Nonulcerative inflammation • Basophilic clusters seen on the surface of intestinal mucosal cells
Microsporidium	• Distortion of villus architecture without inflammation • Small spores with a diagonal or

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Microsporidium	• Distortion of villus architecture without inflammation • Small spores with a diagonal or equatorial belt-like structure
Mycobacterium avium complex	• Necrotizing & non-necrotizing granulomas • Acid-fast staining bacilli are present

Cytomegalovirus (CMV) is the most common viral opportunistic infection of the gastrointestinal tract in patients with advanced AIDS. Initial infection with CMV is usually asymptomatic or similar to Epstein-Barr virus-induced mononucleosis. As with all members of the **herpesvirus family**, latent infection is established after resolution of the initial infection. Reactivation can occur at any time but is most common in the setting of immunosuppression.

In patients with HIV, **CMV colitis** is the second most common reactivation syndrome after CMV retinitis. Patients with CMV colitis have fever, anorexia, weight loss, and abdominal pain. The pain may be vague initially but becomes more localized as the disease progresses. Colonoscopy shows mucosal erythema,

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initially but becomes more localized as the disease progresses. Colonoscopy shows mucosal erythema, erosions, and ulcerations. Histologic examination of biopsy specimens will reveal acute and chronic inflammatory changes, vasculitis, and large cells with large, ovoid nuclei containing **centralized intranuclear basophilic inclusions** (owl's eye appearance).

(Choice A) Patients with advanced AIDS are at risk for disseminated *Mycobacterium avium* complex, which is often associated with diarrhea, abdominal pain, and weight loss. However, acid-fast staining organisms and necrotizing and non-necrotizing granulomas are typically seen on biopsy.

(Choice B) *Cryptosporidium* is a protozoan parasite that causes watery diarrhea in both immunocompromised and immunocompetent patients. However, it primarily affects the small intestine, not the colon. Oocysts can be identified in the stool using microscopy with modified acid-fast stain; biopsy will show basophilic parasites attached to the mucosal brush border.

(Choice C) *Candida albicans* is a normal part of human flora that often causes oropharyngeal and esophageal infections in patients with advanced AIDS. However, *Candida* and other yeasts (eg, *Histoplasma capsulatum*) are a rare cause of colitis.

(Choice E) *Clostridium difficile* is an exotoxin-producing, anaerobic bacterium that can cause severe colitis, most commonly after antibiotic use. Patients usually have fever, abdominal pain, leukocytosis, and diarrhea. Endoscopy is not usually needed but often reveals mucosal pseudomembranes.

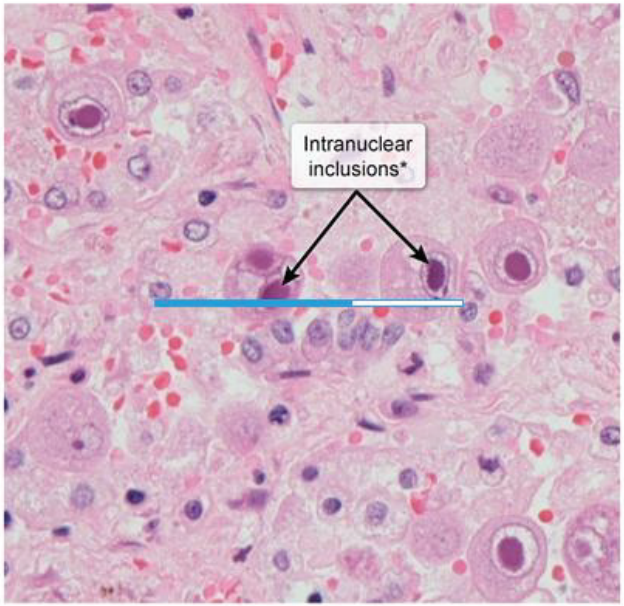
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initially but becomes more localized as the disease progresses. Colonoscopy shows mucosal erythema,

Exhibit Display

Cytomegalovirus



*"Owl's eye" appearance

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(Choice E) *Clostridium difficile* is an exotoxin-producing, anaerobic bacterium that can cause severe colitis, most commonly after antibiotic use. Patients usually have fever, abdominal pain, leukocytosis, and diarrhea. Endoscopy is not usually needed but often reveals mucosal pseudomembranes.

Educational objective:
Cytomegalovirus (CMV) is a common cause of colitis in patients with advanced AIDS. It is the second most common CMV reactivation disease in this population (CMV retinitis is the most common). Patients with CMV colitis often have abdominal pain, fever, diarrhea, and weight loss. Colonoscopy usually shows erythema, erosions, and ulcerations; colonic biopsy typically reveals large cells with prominent basophilic intranuclear inclusions.

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Item 2 of 2

The patient is hospitalized, and appropriate treatment is begun. After discussing the underlying cause of his condition—immunosuppression due to HIV infection—the patient agrees to take antiretroviral therapy consistently. One of the medications in his treatment regimen leads to the production of immature, noninfectious virions containing large polyproteins. Which of the following viral processes is most likely directly inhibited by this agent?

A. Expression of glycoproteins on the virus cell surface
B. Integration of the viral DNA molecule into the host genome
C. Production of functional viral-encoded enzymes
D. Removal of viral template RNA from the RNA-DNA hybrid
E. Translation of virus-encoded regulatory proteins

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Item 2 of 2

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A. ~~Expression of glycoproteins on the virus cell surface~~ (13%)
B. Integration of the viral DNA molecule into the host genome (11%)
✓ C. Production of functional viral-encoded enzymes (58%)
D. ~~Removal of viral template RNA from the RNA-DNA hybrid~~ (5%)
E. ~~Translation of virus-encoded regulatory proteins~~ (11%)

Correct

58%
Answered correctly

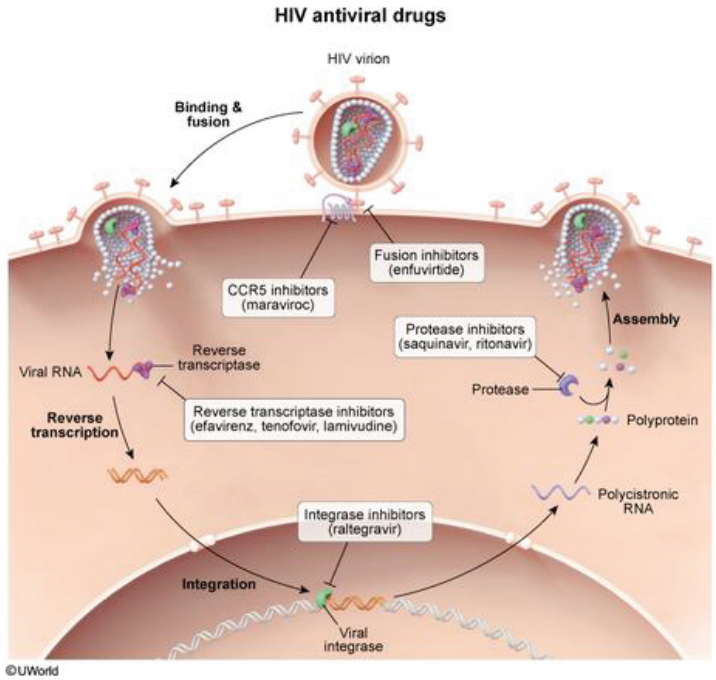
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The **HIV genome** contains 3 major genes (***env***, ***gag***, and ***pol***) that are transcribed as **polycistronic mRNA** and translated into **polyproteins** in the endoplasmic reticulum. The *gag* and *pol* polyprotein products (gag-pol) are **cleaved by HIV protease** into individual HIV enzymes and structural proteins.

Protease inhibitors inhibit HIV protease from cleaving the gag-pol polyproteins, which results in the formation of immature, noninfectious virions due to **impaired production of functional viral proteins**. Protease inhibitors are a common component of first-line HIV antiretroviral therapy and are denoted by medications that end in "navir" (eg, darunavir, atazanavir, ritonavir).

(Choice A) The HIV envelope proteins gp120 and gp41 mediate viral attachment and fusion with the host cell membrane. These proteins are generated as a polyprotein (gp160) from the *env* gene. Unlike the gag-pol polyprotein (which is cleaved by HIV protease) the env polyprotein is cleaved by a host protease, so production of glycosylated viral envelope proteins is not affected by HIV protease inhibitors.

(Choices B and D) The *pol* gene encodes the major HIV enzymes: reverse transcriptase (RT), integrase, and protease. RT converts the HIV RNA genome into complementary double-stranded DNA; it also destroys the HIV RNA genomic template during transcription (ribonuclease H activity). RT is inhibited by nucleoside/nonnucleoside reverse transcriptase inhibitors. Integrase inserts complementary viral DNA into

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and protease. RT converts the HIV RNA genome into complementary double-stranded DNA; it also destroys the HIV RNA genomic template during transcription (ribonuclease H activity). RT is inhibited by nucleoside/nonnucleoside reverse transcriptase inhibitors. Integrase inserts complementary viral DNA into the host chromosome. Integrase strand transfer inhibitors block the function of this enzyme. Both RT and integrase inhibitors block viral replication, but neither are associated with immature virions containing polyproteins.

(Choice E) The HIV genome encodes for several regulatory proteins that are required for viral replication. However, all virus-encoded proteins are translated by host ribosomes, and blockade of protein translation would not be associated with the formation of polyproteins.

Educational objective:

The HIV genome contains 3 major structural genes that are translated as polyproteins and subsequently cleaved by host protease (*env* gene products) or viral protease (*gag-pol* gene products) into the individual proteins that compose the HIV virus. Protease inhibitors block viral protease from cleaving gag-pol polyproteins, which results in the formation of immature virions that are noninfectious.

Microbiology	Infectious Diseases	Antiretroviral therapy
Subject	System	Topic

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A 5-year-old girl is brought to the physician by her parents due to intense perianal itching, especially during the night. The patient is otherwise healthy and her development has been normal. Physical examination shows perianal excoriation. Cellulose adhesive tape is applied to the perianal area shortly after she wakes in the morning. Microscopic analysis of the tape reveals the presence of eggs that are asymmetrically flattened on one side. Which of the following is the most appropriate treatment for this patient's condition?

A. Albendazole
B. Diethylcarbamazine
C. Ivermectin
D. Nifurtimox
E. Praziquantel

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- ✓ A. Albendazole (81%)
- B. Diethylcarbamazine (1%)
- C. Ivermectin (7%)
- D. Nifurtimox (0%)
- E. Praziquantel (8%)

Correct

81%
Answered correctly

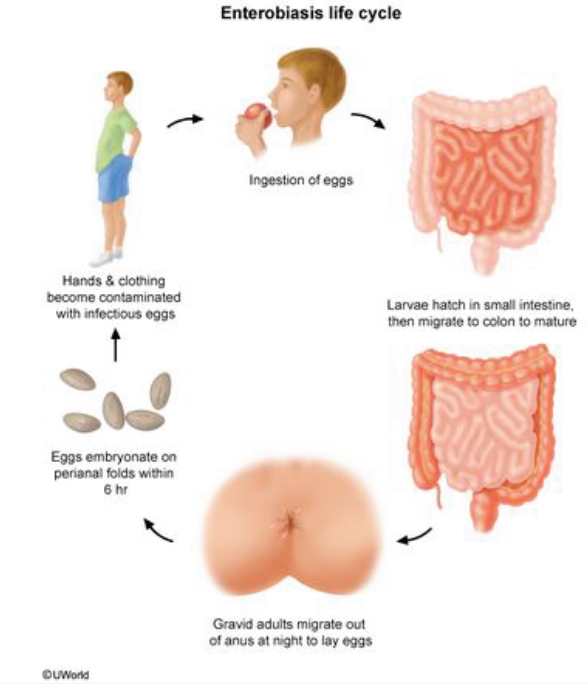
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Enterobiasis, caused by the **pinworm** (*Enterobius vermicularis*), is the most prevalent helminthic infection in the United States and is frequently seen in **children**. The life cycle occurs in the gastrointestinal tract, and the adult worms typically live in the cecum and appendix. In contrast to other worms that release eggs into the intestine, the female **worm migrates to the perianal area at night** to deposit eggs. Larvae mature in the eggs within 6 hours, and the infective eggs can either be ingested by the same individual or spread to other humans. Eggs and worms in the perianal area cause an inflammatory reaction, resulting in **perianal itching** (pruritus ani). Scratching contaminates the hands and furthers transmission.

Diagnosis is made by the **cellulose tape test** (ie, microscopy of adhesive tape applied to the perianal region), which reveals oval eggs flattened on one side. Treatment options include **albendazole**, mebendazole, and pyrantel pamoate.

(Choice B) Diethylcarbamazine is indicated for the treatment of *Loa loa* (loiasis) and *Wuchereria bancrofti* (lymphatic filariasis) infections.

(Choice C) Ivermectin is used to treat infections caused by *Strongyloides stercoralis* (strongyloidiasis) and *Onchocerca volvulus* (onchocerciasis).

(Choice D) Nifurtimox is used to treat diseases caused by trypanosomes, including *Trypanosoma cruzi*

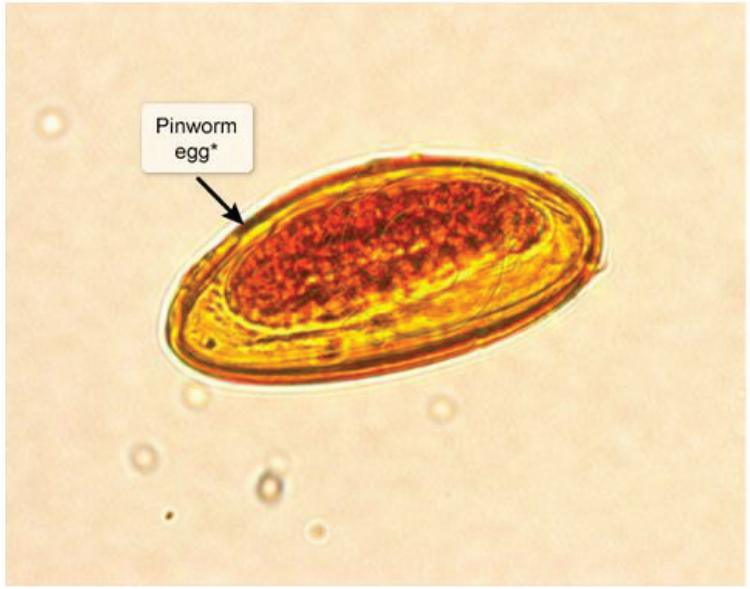
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Enterobius vermicularis



*Identified with tape test

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(Choice D) Nifurtimox is used to treat diseases caused by trypanosomes, including *Trypanosoma cruzi* (Chagas disease).

(Choice E) Infections caused by *Schistosoma* (schistosomiasis), *Clonorchis sinensis* (clonorchiasis), and *Paragonimus westermani* (paragonimiasis) are treated with praziquantel.

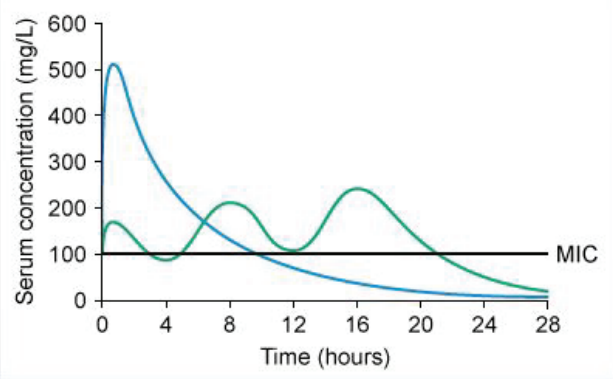
Educational objective:
Enterobius vermicularis infection (enterobiasis) occurs most frequently in children and presents with perianal pruritus. Diagnosis is made by identifying eggs in the perianal region (cellulose tape test). Treatment options include albendazole, mebendazole, and pyrantel pamoate.

Pharmacology	Infectious Diseases	Intestinal helminth parasites
Subject	System	Topic

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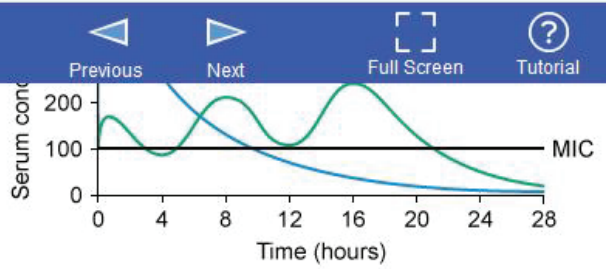
A novel aminoglycoside antibiotic is developed that is intravenously administered and excreted unchanged in urine with an elimination half-life of 4 hours. Two different dosing regimens are tested in a clinical trial: smaller doses given 3 times a day and a higher dose given once a day. The total administered drug amount per kilogram of body weight per day (mg/kg/day) is the same in both regimens. Serum drug concentration is monitored in both groups and is shown in the graph below:

[Blue: once-daily (extended interval) dosing, Green: multiple-daily dosing, MIC: minimum inhibitory concentration]



It is found that both regimens are effective against gram-negative pathogens, with clinical improvement

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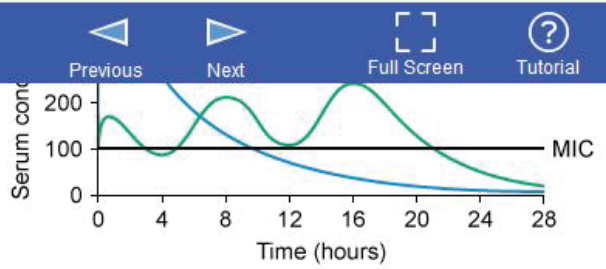
It is found that both regimens are effective against gram-negative pathogens, with clinical improvement occurring slightly earlier on average with once-daily dosing. Which of the following best explains the efficacy of once-daily dosing despite the short half-life of this antibiotic?

A. Concentration-dependent killing
B. High therapeutic index
C. Linear dose–response relationship
D. Low threshold dose
E. Time-dependent killing

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It is found that both regimens are effective against gram-negative pathogens, with clinical improvement occurring slightly earlier on average with once-daily dosing. Which of the following best explains the efficacy of once-daily dosing despite the short half-life of this antibiotic?

- A. Concentration-dependent killing (78%)
- B. High therapeutic index (7%)
- C. Linear dose–response relationship (5%)
- D. Low threshold dose (2%)
- E. Time-dependent killing (6%)

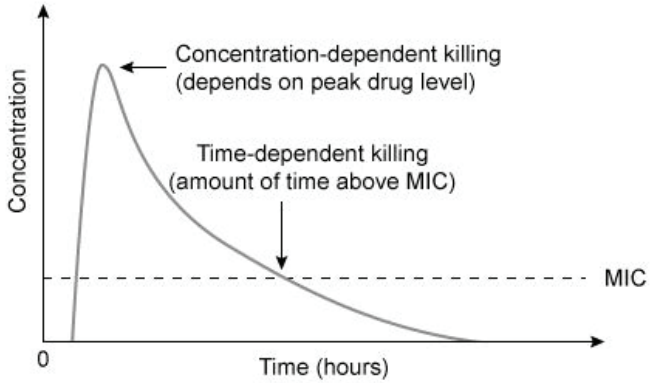
Correct

78%
Answered correctly

24 secs
Time Spent

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The 2 major factors influencing the effectiveness of antimicrobial agents are the drug concentration at the target site and the amount of time that microbes are exposed to the drug. The relative contribution of these factors to drug efficacy depends on the particular agent. In general, antibiotics can be classified into 2 categories based on which factor is more important:

- **Concentration-dependent killing:** Antibiotics with this pattern of activity (eg, aminoglycosides, fluoroquinolones) have a persistent, suppressive effect on bacterial growth following a limited exposure, resulting in increased killing ability when drug levels at the site of infection are maximized. The **higher the peak drug level** compared to the minimum inhibitory concentration (MIC), the **greater**

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The **higher the peak drug level** compared to the minimum inhibitory concentration (MIC), the **greater the antimicrobial activity**. As such, higher-dose, **extended-interval** (ie, once-daily) regimens are frequently used to optimize bacterial killing.

- **Time-dependent killing:** Antibiotics with this activity pattern (eg, beta-lactams [penicillins, cephalosporins], clindamycin) have minimal persistent effects and are dependent on **long exposure durations** for their antimicrobial activity. They are more effective when serum concentrations **exceed the MIC** for a prolonged period. Therefore, more frequent, **multiple-daily dosing** regimens are used to maintain plasma concentrations greater than the MIC for as long as possible.

(Choice B) The therapeutic index (ie, [toxic dose]/[effective dose]) is a measurement of the relative safety of a drug; it is an intrinsic property upon which drug dosing regimens are devised. A relatively high therapeutic index is usually necessary to prevent toxicity with extended-interval dosing because the administered drug amounts lead to higher serum levels than seen with more frequent dosing regimens.

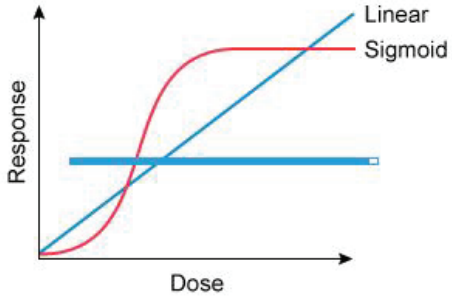
(Choice C) Most drugs exhibit a *sigmoid*-shaped dose response curve that shows no effect until a threshold concentration is exceeded. After this occurs, the effects increase with increasing drug concentration until a saturation threshold (ie, maximum effect) is reached. In contrast to this sigmoidal response, the risk of cancer following exposure to ionizing radiation shows a *linear* dose–response relationship (ie, risk increases proportionately with increased exposure)

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The **higher the peak drug level** compared to the minimum inhibitory concentration (MIC), the **greater**

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relationship (ie, risk increases proportionately with increased exposure)

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concentration until a saturation threshold (ie, maximum effect) is reached. In contrast to this sigmoidal response, the risk of cancer following exposure to ionizing radiation shows a *linear* dose–response relationship (ie, risk increases proportionately with increased exposure).

(Choice D) The threshold dose is the lowest dose at which drug effects are first seen. In this case, both dosing regimens cause serum concentrations to rise above the MIC. Furthermore, the extended-interval dosing regimen results in less total time above the MIC but still demonstrates effectiveness. Therefore, a low dosing threshold does not explain the effectiveness of extended-interval dosing.

(Choice E) In this example, both treatment regimens were effective, with extended-interval dosing having a slightly better response time. Because serum concentrations with the extended-interval regimen remain above the MIC for a much shorter period of time compared to multiple-daily dosing, time-dependent killing does not contribute significantly to overall drug efficacy.

Educational objective:
Antibiotics exhibiting concentration-dependent killing can be administered using relatively high doses given at lower frequency. This allows for effective microbial killing while preventing adverse effects that may occur with prolonged systemic exposure.

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A 6-year-old boy is brought to the office due to persistent cough. His symptoms began with a mild, upper respiratory illness 2 weeks ago, but the cough has progressively worsened, and now spells of dry cough are often followed by vomiting. The patient has no chronic medical conditions but has not received childhood vaccinations due to parental beliefs. He recently returned from a summer camp. On physical examination, the patient is afebrile, and lungs are clear to auscultation. Testing of respiratory secretions shows gram-negative coccobacilli. Which of the following is most likely involved in the pathogenesis of this patient's symptoms?

A. Alveolar influx of polymorphonuclear leukocytes
B. Circulating endotoxin-mediated vasodilation
C. Inflammation and edema of supraglottic tissue
D. Interferon-gamma-induced macrophage activation
E. Loss of ciliated respiratory epithelial cells

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A. Alveolar influx of polymorphonuclear leukocytes (6%)
B. Circulating endotoxin-mediated vasodilation (13%)
C. Inflammation and edema of supraglottic tissue (40%)
D. Interferon-gamma-induced macrophage activation (3%)
E. Loss of ciliated respiratory epithelial cells (35%)

35% 47 secs 03/05/2021

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Bordetella pertussis, a small, gram-negative coccobacillus, spreads rapidly via airborne droplets through communities with low rates of tetanus-diphtheria-pertussis vaccination. Infants and children are most susceptible and typically develop a few weeks of **mucoid rhinorrhea** followed by 2-4 weeks of severe, **paroxysmal cough**, often with an **inspiratory whoop** and subsequent **vomiting**.

Although the bacterium is largely noninvasive, *B pertussis* has several virulence factors (eg, pili, filamentous hemagglutinin, pertactin) that allow it to strongly **attach to respiratory epithelium**. After binding, it then elaborates inflammatory exotoxins, including:

- **Tracheal cytotoxin** – directly damages and **destroys ciliated epithelial cells**, leading to a loss of airway protection, subsequent microaspiration, and development of the characteristic paroxysmal cough.
- **Pertussis toxin** – an AB toxin that enters cells and activates adenylate cyclase, leading to alterations in cellular signaling that **inhibit phagocyte activity** and can cause lymphocytosis.

(Choice A) Acute bacterial pneumonia (eg, *Streptococcus pneumoniae*) presents with fever and productive cough; it is associated with massive migration of neutrophils from the bloodstream into the alveoli. In contrast, pertussis is associated with reduced neutrophil influx due to elaboration of pertussis

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(Choice A) Acute bacterial pneumonia (eg, *Streptococcus pneumoniae*) presents with fever and productive cough; it is associated with massive migration of neutrophils from the bloodstream into the alveoli. In contrast, pertussis is associated with reduced neutrophil influx due to elaboration of pertussis toxin and adenylate cyclase toxin.

(Choice B) Endotoxins are cell-wall components of gram-negative bacteria that can cause septic shock (eg, hypotension, fever, diminished pulses) when released into the bloodstream. Pertussis is noninvasive; disease manifestations are mediated by exotoxins, not endotoxins.

(Choice C) *Haemophilus influenzae* is a small, gram-negative coccobacillus that often causes infection in patients who have not been vaccinated (*H influenzae* type B vaccine). It is a leading cause of epiglottitis, which typically presents with respiratory distress, tripod posture, and anxiousness. Cough is usually absent.

(Choice D) *Mycobacterium tuberculosis* infection is marked by interferon-gamma–mediated macrophage activation, which leads to the formation of protective granulomas and the killing of the bacteria. *M tuberculosis* is an acid-fast bacterium; it is not gram-negative.

Educational objective:

Bordetella pertussis, a small, gram-negative coccobacillus, can cause outbreaks of whooping cough in

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disease manifestations are mediated by exotoxins, not endotoxins.

(Choice C) *Haemophilus influenzae* is a small, gram-negative coccobacillus that often causes infection in patients who have not been vaccinated (*H influenzae* type B vaccine). It is a leading cause of epiglottitis, which typically presents with respiratory distress, tripod posture, and anxiousness. Cough is usually absent.

(Choice D) *Mycobacterium tuberculosis* infection is marked by interferon-gamma–mediated macrophage activation, which leads to the formation of protective granulomas and the killing of the bacteria. *M tuberculosis* is an acid-fast bacterium; it is not gram-negative.

Educational objective:

Bordetella pertussis, a small, gram-negative coccobacillus, can cause outbreaks of whooping cough in unvaccinated individuals. Infected infants and children generally develop mucoid rhinorrhea followed by severe, paroxysmal cough that may be associated with an inspiratory whoop and vomiting. The bacterium is largely noninvasive and secretes several exotoxins that severely damage ciliated respiratory epithelium.

Microbiology	Infectious Diseases	Pertussis
Subject	System	Topic

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A 25-year-old man with multiple injuries sustained in a motorcycle accident develops osteomyelitis while in the hospital. The organism is identified as methicillin-sensitive *Staphylococcus aureus*, and antibiotics are started. Which of the following is the most important measure to reduce the risk of transmission to other patients?

A. Contact precautions
B. Hand hygiene
C. Isolation precautions
D. Masks
E. Restricting visitors

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A 25-year-old man with multiple injuries sustained in a motorcycle accident develops osteomyelitis while in the hospital. The organism is identified as methicillin-sensitive *Staphylococcus aureus*, and antibiotics are started. Which of the following is the most important measure to reduce the risk of transmission to other patients?

A. Contact precautions (16%)
✓ B. Hand hygiene (69%)
C. ~~Isolation precautions~~ (6%)
D. ~~Masks~~ (6%)
E. ~~Restricting visitors~~ (0%)

Correct

69%
Answered correctly

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Explanation

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Hand hygiene by health care workers is the single most important measure to reduce the risk of transmission of microorganisms between patients. It includes handwashing with soap and water or using alcohol-based hand sanitizers that do not require water. Proper handwashing technique involves washing all surfaces of the hands and fingers with soap and water for at least 15 seconds, drying with a disposable towel, and using the towel to turn off the faucet. Alcohol-based hand sanitizer should cover all surfaces of the hands and fingers and be allowed to dry. The World Health Organization recommends handwashing before and after touching a patient, before aseptic procedures, and after contact with body fluids or patient surroundings.

(Choice A) Contact precautions involve wearing nonsterile gloves for all patient contact and gowns during substantial contact with infective material. These precautions are indicated when caring for patients with specific multidrug-resistant bacteria (eg, methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci) or with certain parasitic or viral pathogens. This patient's **methicillin-sensitive** *Staphylococcus aureus* infection does not require use of contact precautions.

(Choice C) Isolation precautions are indicated in the care of patients with infectious airborne diseases (eg, tuberculosis) and involve a private airborne infection isolation room with negative air pressure, closed doors, and the use of specialized particulate respirator masks.

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sensitive *Staphylococcus aureus* infection does not require use of contact precautions.

(Choice C) Isolation precautions are indicated in the care of patients with infectious airborne diseases (eg, tuberculosis) and involve a private airborne infection isolation room with negative air pressure, closed doors, and the use of specialized particulate respirator masks.

(Choice D) Facemasks are used as a barrier for respiratory secretions and are not a substitute for hand-washing.

(Choice E) Restricting visitors is unnecessary, although all visitors should wash their hands before and after contact with the patient.

Educational objective:
Hand hygiene is the single most important measure to reduce the risk of transmission of hospital-acquired infections.

References

- Update on hand hygiene.

Microbiology	Infectious Diseases	Infection control
Subject	System	Topic

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A 23-year-old woman comes to the emergency department due to 2 hours of fever, chills, headache, and myalgias. Earlier in the day, the patient saw her primary care physician for a genital ulcer. She underwent testing for sexually transmitted infections and was found to have a positive VDRL and fluorescent treponemal antibody absorption test. The remainder of her testing was negative. The patient received an intramuscular injection of benzathine penicillin G, and several hours later her current symptoms began. Temperature is 38 C (100.4 F), blood pressure is 120/70 mm Hg, and pulse is 92/min and regular. Lung sounds are normal. There is an indurated, nontender vulval ulcer and several enlarged inguinal lymph nodes. No other skin rash is present. Which of the following is the most likely cause of this patient's current symptoms?

A. Conjugation of antibiotic and host antigens
B. Disease progression due to antibiotic resistance
C. Drug-induced bacterial cell wall disintegration
D. Immune sensitization from prior penicillin exposure
E. Poor renal tubular excretion of the drug

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A. Conjugation of antibiotic and host antigens (7%)
B. Disease progression due to antibiotic resistance (2%)
C. Drug-induced bacterial cell wall disintegration (75%)
D. Immune sensitization from prior penicillin exposure (12%)
E. Poor renal tubular excretion of the drug (0%)

Correct
75%
01 min, 08 secs
11/04/2020

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Jarisch-Herxheimer reaction	
Epidemiology	• 6-48 hr after initiating treatment for syphilis (most commonly primary or secondary) • May also be seen with treatment of other spirochetes (eg, Lyme disease, leptospirosis) or atypical (eg, *Bartonella*) organisms
Pathogenesis	• Massive destruction of organisms → lipoproteins released into the circulation → transient inflammatory response
Clinical presentation	• Acute onset of fever, chills, myalgias • Rash progression in secondary syphilis

This patient with a genital ulcer, inguinal lymphadenopathy, and positive nontreponemal/treponemal testing was treated for primary **syphilis** with intramuscular **benzathine penicillin G**. She then developed an acute febrile syndrome (fever, chills, myalgia, headache) a few hours later, raising strong suspicion for the

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This patient with a genital ulcer, inguinal lymphadenopathy, and positive nontreponemal/treponemal testing was treated for primary **syphilis** with intramuscular **benzathine penicillin G**. She then developed an acute febrile syndrome (fever, chills, myalgia, headache) a few hours later, raising strong suspicion for the **Jarisch-Herxheimer reaction**. This systemic inflammatory response occurs within hours of **antibiotic initiation** for spirochetal infections (eg, syphilis, Lyme disease, leptospirosis). The **rapid lysis of spirochetes** spills bacterial lipoproteins into the bloodstream and triggers a strong innate immunologic response. Most cases are self-limited and do not require intervention.

(Choice A) Conjugation of antibiotic and host antigens can cause drug-induced fever, which typically arises several days or a few weeks (not within hours) after drug initiation. Patients often have fever and rash.

(Choice B) Syphilis is universally susceptible to penicillin. In addition, secondary syphilis (eg, widespread maculopapular rash, constitutional symptoms, lymphadenopathy) develops weeks or months after the chancre of primary syphilis; therefore, disease progression is unlikely in this case.

(Choice D) Penicillin allergy is due to immune sensitization following previous exposure. Additional exposure triggers an IgE-mediated (type I) allergic response; symptoms often include rash, bronchospasm, angioedema, flushing, hypotension, and/or pruritis. Fever, chills, headache, and myalgias would be

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chancre of primary syphilis; therefore, disease progression is unlikely in this case.

(Choice D) Penicillin allergy is due to immune sensitization following previous exposure. Additional exposure triggers an IgE-mediated (type I) allergic response; symptoms often include rash, bronchospasm, angioedema, flushing, hypotension, and/or pruritis. Fever, chills, headache, and myalgias would be atypical and are more consistent with the Jarisch-Herxheimer reaction.

(Choice E) Intramuscular benzathine penicillin G is a long-acting drug that is excreted in the urine. Poor renal tubular secretion could increase plasma drug concentrations but would be unlikely to induce a systemic inflammatory response.

Educational objective:

The Jarisch-Herxheimer reaction is an acute inflammatory reaction that occurs within hours of treatment for spirochetal infections (eg, syphilis). The rapid lysis of spirochetes releases inflammatory bacterial lipoproteins into the circulation and causes acute fever, rigors, and myalgias.

Pharmacology	Infectious Diseases	Syphilis
Subject	System	Topic

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An outbreak of hepatitis in New Delhi was characterized by high incidence of fulminant hepatitis in pregnant women, who experienced a mortality rate of 20%. The virus responsible for the outbreak:

A. Is an unenveloped RNA virus
B. Is transmitted parenterally
C. Is associated with chronic hepatitis
D. Infects only HBsAg-positive individuals
E. Has oncogenic properties

Submit

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An outbreak of hepatitis in New Delhi was characterized by high incidence of fulminant hepatitis in pregnant women, who experienced a mortality rate of 20%. The virus responsible for the outbreak:

- A. Is an unenveloped RNA virus (64%)
- B. ~~Is transmitted parenterally~~ (11%)
- C. ~~Is associated with chronic hepatitis~~ (6%)
- D. Infects only HBsAg-positive individuals (14%)
- E. ~~Has oncogenic properties~~ (3%)

Correct

64%
Answered correctly

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01/30/2021
Last Updated

Explanation

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Hepatitis E virus is an unenveloped, single-stranded RNA virus spread through the fecal-oral route. Infection with HEV occurs primarily in young and middle-aged adults living in Asia, sub-Saharan Africa, and Mexico, with an average incubation period of six weeks. While the virus is shed in the stool during the acute illness, the disease is typically self-limited and not associated with either chronic liver disease or a carrier state. HEV Ag or HEV RNA can be detected in the stool or liver in the earliest stages of infection (when the patient is asymptomatic). Later, serum transaminases and IgM anti-HEV titers rise in association with clinical illness. The most concerning feature of hepatitis E is the high mortality rate observed in infected pregnant women.

(Choice B) While hepatitis B, C, and D can be transmitted parenterally (with intravenous drug abusers and hemophiliacs are particularly high risk), hepatitis A and E are primarily transmitted via the fecal-oral route.

(Choice C) Hepatitis E causes an acute illness and is not associated with chronic infection.

(Choice D) Unlike hepatitis D virus, hepatitis E is not dependent on HBsAg for infection and multiplication.

(Choice E) Because of their association with hepatocellular carcinoma, hepatitis B and C have been suggested to have oncogenic properties. Hepatitis E is not associated with an increased risk of hepatocellular carcinoma, however.

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infected pregnant women.

(Choice B) While hepatitis B, C, and D can be transmitted parenterally (with intravenous drug abusers and hemophiliacs are particularly high risk), hepatitis A and E are primarily transmitted via the fecal-oral route.

(Choice C) Hepatitis E causes an acute illness and is not associated with chronic infection.

(Choice D) Unlike hepatitis D virus, hepatitis E is not dependent on HBsAg for infection and multiplication.

(Choice E) Because of their association with hepatocellular carcinoma, hepatitis B and C have been suggested to have oncogenic properties. Hepatitis E is not associated with an increased risk of hepatocellular carcinoma, however.

Educational Objective:
Hepatitis E virus is an unenveloped, single-stranded RNA virus spread through the fecal-oral route. The most concerning feature of hepatitis E infection is the high mortality rate observed in infected pregnant women.

Microbiology	Infectious Diseases	Hepatitis e
Subject	System	Topic

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A 76-year-old hospitalized woman is evaluated for persistent fevers. Four days ago, she was admitted to the hospital for sepsis, for which she has received broad-spectrum empiric intravenous antibiotic therapy. Her temperature is 38.9 C (102 F), blood pressure is 110/80 mm Hg, pulse is 98/min, and respirations are 18/min. Cardiac examination reveals a new diastolic murmur. Multiple blood cultures drawn at different times grow *Enterococcus*. Echocardiogram reveals mitral valve vegetation suggestive of endocarditis. An intravenous antibiotic is added to the patient's treatment regimen for synergy. Several days later, she develops tinnitus and hearing loss attributed to this antibiotic. The additional antibiotic most directly affects which of the following processes?

A. Cell wall cross-linking
B. DNA unwinding
C. Folic acid synthesis
D. Maintenance of transmembrane potential
E. mRNA genetic code reading
F. tRNA charging

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Her temperature is 38.9 C (102 F), blood pressure is 110/80 mm Hg, pulse is 98/min, and respirations are 18/min. Cardiac examination reveals a new diastolic murmur. Multiple blood cultures drawn at different times grow *Enterococcus*. Echocardiogram reveals mitral valve vegetation suggestive of endocarditis. An intravenous antibiotic is added to the patient's treatment regimen for synergy. Several days later, she develops tinnitus and hearing loss attributed to this antibiotic. The additional antibiotic most directly affects which of the following processes?

A. ~~Cell wall cross-linking~~ (18%)
B. ~~DNA unwinding~~ (5%)
C. ~~Folic acid synthesis~~ (4%)
D. ~~Maintenance of transmembrane potential~~ (5%)
E. mRNA genetic code reading (54%)
F. tRNA charging (10%)

Correct

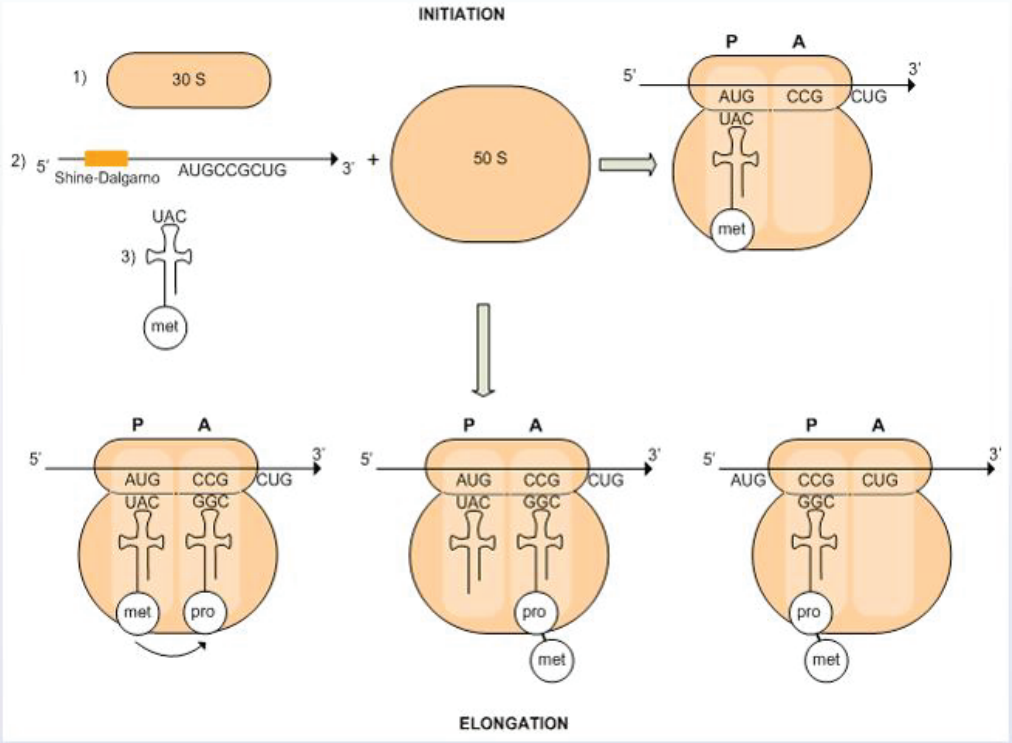
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This patient with enterococcal endocarditis likely received an **aminoglycoside** (AG) such as gentamicin, a

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ELONGATION

This patient with enterococcal endocarditis likely received an **aminoglycoside** (AG) such as gentamicin, a ribosome-targeting antibiotic. AGs are associated with **ototoxicity** (hearing loss, tinnitus) and **nephrotoxicity**.

mRNA is translated into amino acids (AAs) and proteins on ribosomes.

- The small ribosomal subunit (30S in prokaryotes, 40S in eukaryotes) binds mRNA, which contains genetic information serving as a reading frame, and tRNA, which serves as an AA carrier
- The larger ribosomal subunit (50S in prokaryotes, 60S in eukaryotes) contains peptidyltransferase, which catalyzes peptide bond formation between AAs

In **prokaryotes**, a unique mRNA sequence (Shine-Dalgarno) is located upstream from initiation codon AUG, which recognizes an N-formylmethionine-tRNA. This sequence allows 30S binding to mRNA and this N-formylmethionine-tRNA (forming the prokaryotic 30S **initiation complex**). The energy for this reaction (GTP hydrolysis) brings the 50S subunit into the initiation complex, resulting in a 70S ribosomal unit.

AGs irreversibly bind to **bacterial 30S** but not eukaryotic 40S; this causes **genetic code misreading** and bacterial protein synthesis inhibition. AGs also appear to impact **translocation**, whereby an aminoacyl-

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unit.

AGs irreversibly bind to **bacterial 30S** but not eukaryotic 40S; this causes **genetic code misreading** and bacterial protein synthesis inhibition. AGs also appear to impact **translocation**, whereby an aminoacyl-tRNA is shifted from the ribosomal A site (after initial binding) to the P site (after AA incorporation into the peptide chain during elongation) to the E site (after AA cleaving from its tRNA). The initial N-formylmethionine-tRNA notably binds at the P site.

(Choice A) AGs need to diffuse inside the cell to reach the ribosome. As a result, they are often prescribed **synergistically** in combination with antibiotics affecting cell wall synthesis. These include penicillins, which impact cell wall cross-linking, or vancomycin. Vancomycin is also associated with ototoxicity, but it is a glycopeptide antibiotic that acts by **directly** inhibiting peptidoglycan synthesis, **not** cell wall cross-linking (which occurs at a later stage of cell wall synthesis). Although *Enterococcus* is generally resistant to AGs, these drugs are routinely used as synergistic agents **in combination** with penicillins or vancomycin in patients with enterococcal endocarditis; such combinations lead to improved bacterial killing and are the standard of care for this condition.

(Choices B and C) Fluoroquinolones act on DNA gyrase to prevent DNA unwinding. Trimethoprim-sulfamethoxazole affects folic acid synthesis. These antibiotics are not classically associated with

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and are the standard of care for this condition.

(Choices B and C) Fluoroquinolones act on DNA gyrase to prevent DNA unwinding. Trimethoprim-sulfamethoxazole affects folic acid synthesis. These antibiotics are not classically associated with ototoxicity and are not used synergistically for enterococcal endocarditis.

(Choice D) Daptomycin disrupts the bacterial membrane by creating transmembrane channels that cause intracellular ion leakage and cellular membrane depolarization. Its main side effects are myopathy and rhabdomyolysis.

(Choice F) tRNA charging refers to initial covalent bonding between tRNA and the corresponding AA, facilitated by aminoacyl-tRNA synthetase; inhibitors of this enzyme are potential antibiotics.

Educational objective:
Aminoglycosides inhibit genetic code reading and protein synthesis by binding to the prokaryotic 30S ribosomal subunit.

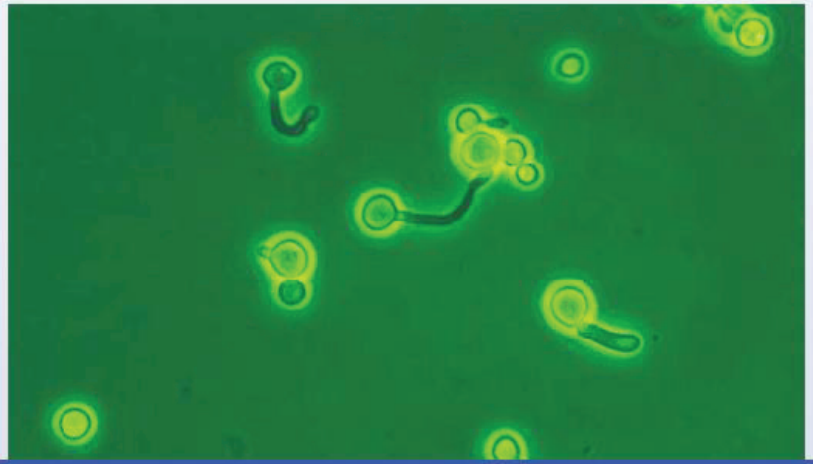
Pharmacology	Infectious Diseases	Aminoglycoside
Subject	System	Topic

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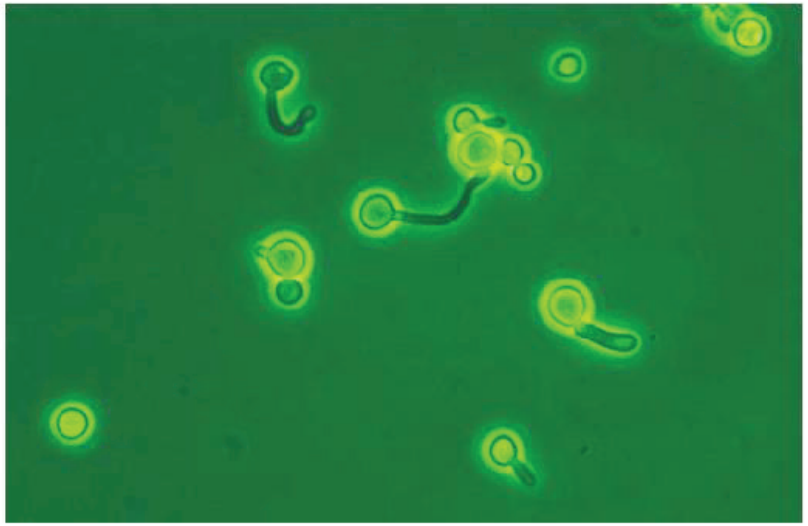
A 32-year-old man was referred to a hematologist 6 months ago with complaints of fatigue, night sweats, and difficulty breathing while lying supine. He also reported a 20 lb (9 kg) weight loss over the last 6 weeks, although he denied any alterations in his diet. On physical examination, enlarged lymph nodes were palpated in his neck and groin and a complete diagnostic work-up was ordered. Pathology slides revealed Reed Sternberg cells and a diagnosis of Hodgkin's lymphoma was made. The patient then began an aggressive chemotherapy regimen. During one of his treatment cycles, the patient experiences fever, dyspnea, and malaise. Blood cultures incubated for 3 hours at 37 C (98.6 F) reveal the following findings:



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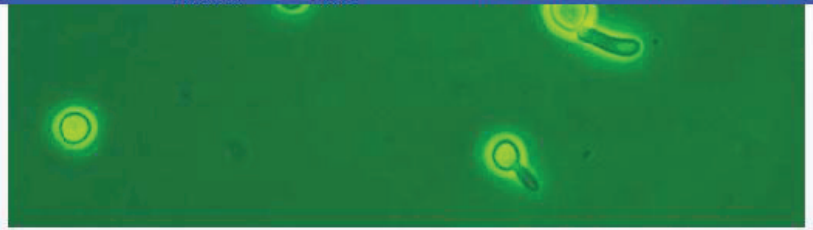
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Which of the following is the most likely cause of this patient's condition?

A. *Rhizopus* species

B. *Aspergillus fumigatus*

C. *Candida albicans*

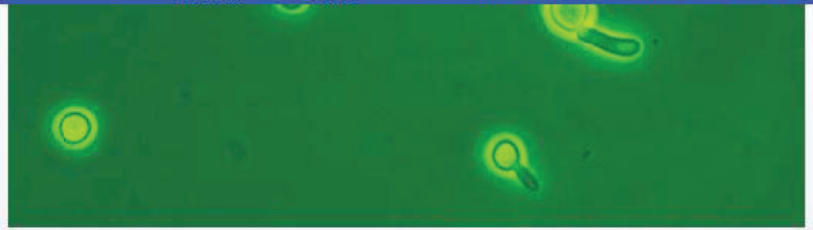
D. *Cryptococcus neoformans*

E. *Histoplasma capsulatum*

F. *Coccidioides immitis*

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Which of the following is the most likely cause of this patient's condition?

- A. *Rhizopus* species (5%)
- B. *Aspergillus fumigatus* (6%)
- ✓ C. *Candida albicans* (44%)
- D. *Cryptococcus neoformans* (32%)
- E. *Histoplasma capsulatum* (5%)
- F. *Coccidioides immitis* (5%)

Correct

44%

20 secs

10/05/2020

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Candida fungi exist in yeast (single cell) form. On light microscopy, they appear as budding yeasts with pseudohyphae. The germ tube test is diagnostic of *Candida albicans*, and allows it to be distinguished from other members of the *Candida* family (such as *C. tropicalis* and *C. glabrata*). Inoculation of *Candida albicans* into serum at 37 C (98.6 F) for 3 hours leads to the formation of true hyphae from the yeast, as shown in the microscopic image above. These growing hyphae are called "germ tubes."

Candida species are a part of the normal human skin and mucous membrane flora. *Candida* can cause localized disease in immunocompetent people with decreased local defenses. Potential manifestations include:

1. **Oral thrush**. White patches form on the oral mucosa in patients who wear dentures, frequently use antibiotics or inhaled steroids, or have diabetes mellitus. They may be asymptomatic or experience burning pain.
2. **Vulvovaginal candidiasis**. Patients complain of vulvar pruritus and vaginal discharge. Physical examination reveals vulvar erythema and a thick white vaginal discharge. This condition is associated with antibiotic use, diabetes mellitus, and contraceptive use.
3. **Cutaneous candidiasis.** This can occur in areas exposed to heat or high humidity (e.g., dishwashers' hands, infants' groins, etc.). Signs include erythema, a vesiculopapular rash, maceration, and

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with antibiotic use, diabetes mellitus, and contraceptive use.

3. **Cutaneous candidiasis.** This can occur in areas exposed to heat or high humidity (e.g., dishwashers' hands, infants' groins, etc.). Signs include erythema, a vesiculopapular rash, maceration, and fissuring.

In immunocompromised patients, *Candida* can also cause disseminated disease that may affect any organ system. Potential manifestations include pneumonia, esophagitis, right-sided endocarditis, abscesses, and candidemia (sepsis).

(Choices A and B) *Rhizopus* and *Aspergillus* exist only in mold form (forming true hyphae). Germ tubes are not seen.

(Choice D) *Cryptococcus neoformans* classically causes meningitis and lung infections in AIDS patients. It is an oval budding yeast with a thick capsule that can mimic the appearance of *Candida* species, although *Cryptococcus* typically does not form hyphae or pseudohyphae. India ink stain of the CSF reveals a wide clear zone around the nucleus (corresponds to unstained capsule).

(Choice E) *Histoplasma capsulatum* is a dimorphic fungus that exists in yeast form at body temperature. Microscopic examination of tissue specimens would reveal oval yeast cells within macrophages. *Histoplasma* does not form germ tubes.

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It is an oval budding yeast with a thick capsule that can mimic the appearance of *Candida* species, although *Cryptococcus* typically does not form hyphae or pseudohyphae. India ink stain of the CSF reveals a wide clear zone around the nucleus (corresponds to unstained capsule).

(Choice E) *Histoplasma capsulatum* is a dimorphic fungus that exists in yeast form at body temperature. Microscopic examination of tissue specimens would reveal oval yeast cells within macrophages. *Histoplasma* does not form germ tubes.

(Choice F) *Coccidioides immitis* is a dimorphic fungus that forms molds at 25 C (77 F), but exists as spherules in human tissues. Spherules are covered by a capsule and contain endospores. Germ tubes are not formed.

Educational objective:

Candida albicans is the most common cause of opportunistic mycosis. It can affect any organ and cause generalized candidemia. Yeasts and pseudohyphae on light microscopy and a positive germ tube test are diagnostic of *Candida albicans* infection.

References

- Current treatment strategies for disseminated candidiasis.
- Utility of the germ tube test for direct identification of Candida albicans from positive blood cultures

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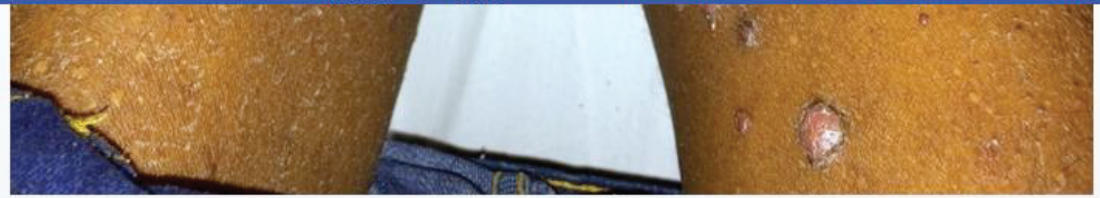
A 45-year-old woman with HIV comes to the office due to the appearance of multiple tender nodules on her lower extremities over the past several weeks. The patient tried to squeeze open the lesions, but this led to profuse bleeding with no expression of pus. She works at a pet store in Mississippi and has regular contact with a variety of animals. Skin examination findings are shown below.



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Biopsy of the lesions reveals large endothelial cells forming vascular channels with a mixed neutrophilic and lymphocytic infiltrate. Immunohistochemical staining for human herpesvirus 8 is negative. Infection with which of the following pathogens is most likely responsible for this patient's skin condition?

A. *Actinomyces israelii*

B. *Bartonella henselae*

C. *Blastomyces dermatitidis*

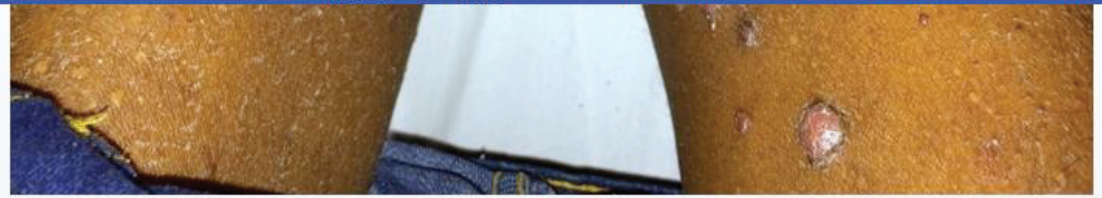
D. *Mycobacterium marinum*

E. *Staphylococcus aureus*

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Biopsy of the lesions reveals large endothelial cells forming vascular channels with a mixed neutrophilic and lymphocytic infiltrate. Immunohistochemical staining for human herpesvirus 8 is negative. Infection with which of the following pathogens is most likely responsible for this patient's skin condition?

A. *Actinomyces israelii* (2%)
✓ B. *Bartonella henselae* (76%)
C. *Blastomyces dermatitidis* (14%)
D. *Mycobacterium marinum* (5%)
E. *Staphylococcus aureus* (1%)

Correct

76%

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Bacillary angiomatosis (BA) is characterized by the formation of highly vascular lesions in the skin and other organs due to infection with the small, gram-negative bacterium ***Bartonella henselae***. The major reservoir for this organism is domesticated cats, and transmission to humans primarily occurs after a **cat scratch** or bite. Patients with intact immunity who are exposed to *B henselae* often develop cat-scratch disease (regional lymphadenopathy), but those with **advanced AIDS** are at risk for the more severe clinical syndrome of BA.

Patients with BA develop **violaceous**, **cutaneous lesions** that are highly vascular. Lesions form over weeks or months and are typically associated with fever, weight loss, and other constitutional symptoms. As these lesions are similar to those seen in Kaposi sarcoma, tissue testing for human herpesvirus 8 (HHV-8) is typically performed (HHV-8 testing will be positive in Kaposi sarcoma and negative in BA). Biopsy with histopathology confirms the diagnosis and usually reveals large endothelial cells forming **small vascular channels** surrounded by a mixed inflammatory infiltrate. Modified silver stain can also identify the organism.

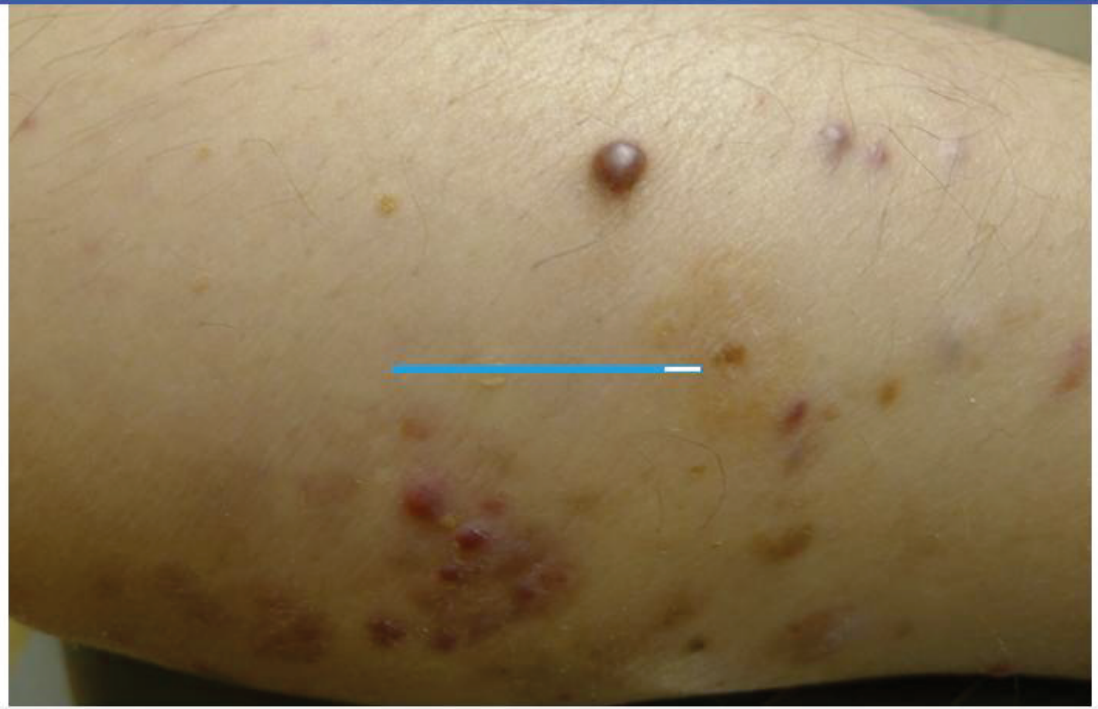
(Choice A) *Actinomyces israelii* is a branching, gram-positive bacterium that grows in filaments. It primarily causes a cervicofacial infection that begins as a slowly growing mass which evolves into multiple abscesses and draining sinus tracts with yellow ("sulfur") granules. Histopathology typically shows chronic

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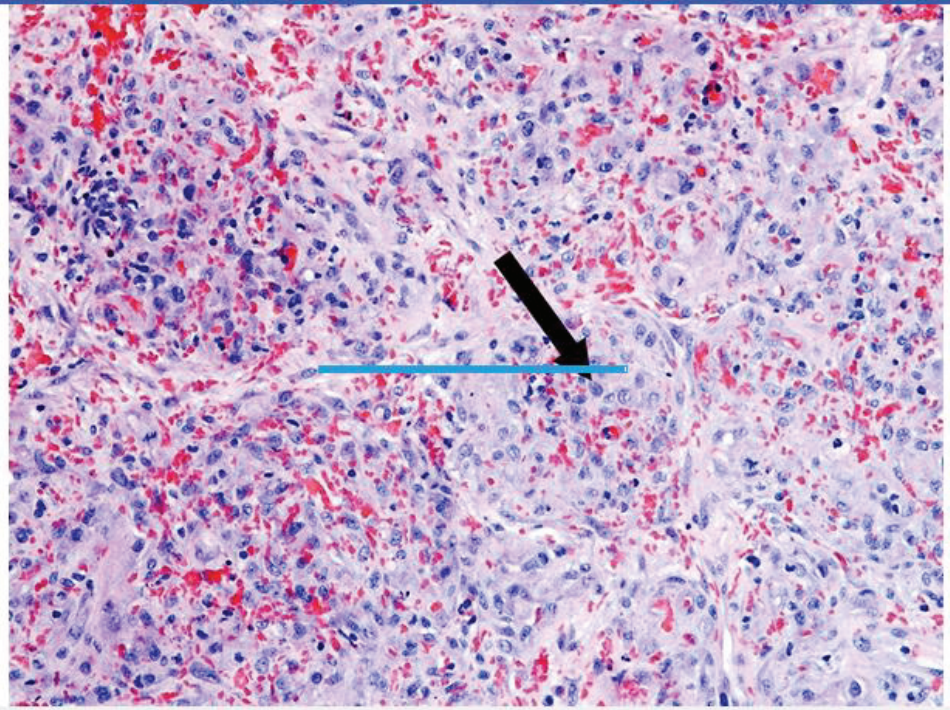
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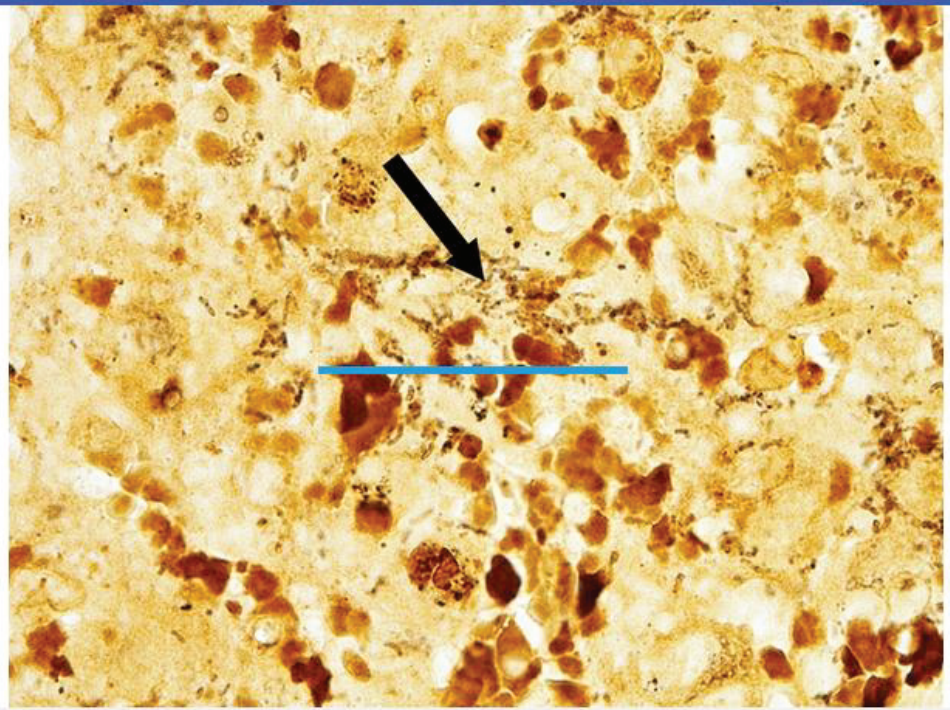
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(Choice A) *Actinomyces israelii* is a branching, gram-positive bacterium that grows in filaments. It primarily causes a cervicofacial infection that begins as a slowly growing mass which evolves into multiple abscesses and draining sinus tracts with yellow ("sulfur") granules. Histopathology typically shows chronic inflammatory granulation tissue surrounding dense fibrosis.

(Choice C) *Blastomyces dermatitidis* is a dimorphic fungus that primarily causes acute or chronic pneumonia but can also spread to the skin, leading to verrucous lesions with irregular borders. Culture is usually required for diagnosis and histology will show granulomas.

(Choice D) *Mycobacterium marinum* is a nontuberculous mycobacterium that is found in fresh and salt water. It can inoculate areas of broken skin (eg, abrasions) and result in an infection marked by cutaneous papules, ulcers, and scarring. Histology reveals granulomatous inflammation.

(Choice E) *Staphylococcus aureus* skin infections (eg, folliculitis) are more common in patients with HIV. However, these infections typically develop over a few days and are associated with purulent fluid.

Educational objective:
Bacillary angiomatosis is primarily seen in patients with advanced AIDS. It is caused by the gram-negative bacterium *Bartonella henselae*, which is typically transmitted by a cat scratch. Patients usually develop highly vascular, violaceous, cutaneous lesions over weeks or months. Histology of the lesions reveals

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(Choice C) *Blastomyces dermatitidis* is a dimorphic fungus that primarily causes acute or chronic pneumonia but can also spread to the skin, leading to verrucous lesions with irregular borders. Culture is usually required for diagnosis and histology will show granulomas.

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Educational objective:
Bacillary angiomatosis is primarily seen in patients with advanced AIDS. It is caused by the gram-negative bacterium *Bartonella henselae*, which is typically transmitted by a cat scratch. Patients usually develop highly vascular, violaceous, cutaneous lesions over weeks or months. Histology of the lesions reveals large endothelial cells forming small vascular channels with a surrounding inflammatory infiltrate.

Microbiology	Infectious Diseases	Bartonella
Subject	System	Topic

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A 17-year-old boy is hospitalized with recent-onset insomnia, headaches, periodic agitation, and dysphagia. He is a high school student interested in becoming a veterinarian. He owns a snake, fish, and parrot and, about 4 weeks ago, went on a field trip to study bats in a cave. The patient has no known medical problems and is not taking any medications. He does not consume alcohol and has never used illicit drugs. Despite hospitalization and treatment, he develops painful spasms, progressive paralysis, and coma and dies. Which of the following interventions would have most likely prevented this student from developing this illness?

A. Cellular receptor inhibitor drug
B. Inactivated vaccine
C. Interferon therapy
D. Live attenuated vaccine
E. Toxoid vaccine
F. Viral enzyme inhibitor drug

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dysphagia. He is a high school student interested in becoming a veterinarian. He owns a snake, fish, and parrot and, about 4 weeks ago, went on a field trip to study bats in a cave. The patient has no known medical problems and is not taking any medications. He does not consume alcohol and has never used illicit drugs. Despite hospitalization and treatment, he develops painful spasms, progressive paralysis, and coma and dies. Which of the following interventions would have most likely prevented this student from developing this illness?

A. Cellular receptor inhibitor drug (5%)
B. Inactivated vaccine (47%)
C. Interferon therapy (5%)
D. Live attenuated vaccine (11%)
E. Toxoid vaccine (26%)
F. Viral enzyme inhibitor drug (2%)

Correct
47%
01 min, 19 secs
03/26/2021

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Human rabies		
Pathogenesis	• Transmission of rabies virus by a bite from an infected mammal	
Reservoir	• United States: bats (most common), raccoons, skunks, foxes • Developing world: dogs	
Clinical features	**Encephalitic**	• Hydrophobia & aerophobia (due to pharyngeal spasm) • Autonomic instability • Spasticity • Agitation & altered mental status
	Paralytic	• Ascending flaccid paralysis
Postexposure prophylaxis*	• Rabies immunoglobulin • Rabies vaccine series	
Prognosis	• Coma, respiratory failure & death within weeks	

*In cases of a high-risk animal that cannot be tested or observed.

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Restlessness, agitation, and dysphagia progressing to coma within weeks of exploring a bat cave is concerning for **rabies encephalitis**. Although **bats** (and, almost as commonly, raccoons) are among the main sources of rabies in the United States, many patients with bat rabies are not aware that they had been bitten. Once in a wound, the virus travels retrograde via peripheral nerves to the dorsal root ganglia and then to the brain, where replication occurs. The virus then spreads to other organs through neural pathways. Common manifestations include a nonspecific, flu-like prodrome followed by an acute neurologic syndrome with agitation, persistent fever, variable consciousness, and painful **spasms** with swallowing or inspiration (causing dysphagia, hydrophobia, and aerophobia). Generalized flaccid paralysis and coma ensue, with most patients dying within weeks.

Prophylactic vaccination is recommended for individuals at high exposure risk (eg, veterinarians, cave explorers, laboratory workers handling infected tissues, travelers to countries where rabid dogs are prevalent). **Postexposure prophylaxis** (a medical emergency) generally includes rabies immune globulin and vaccination; it is not effective after symptom onset. The approved rabies **vaccines** consist of various rhabdovirus strains grown in tissue cell culture and **inactivated** by beta-propiolactone.

(Choices A, C, and F) No antirabies drugs targeting specific viral pathways (eg, cellular entry) are available, and interferon is not used in rabies management.

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(Choices A, C, and F) No antirabies drugs targeting specific viral pathways (eg, cellular entry) are available, and interferon is not used in rabies management.

(Choice D) Some live attenuated rabies vaccines have been used in wild animal populations, but none are currently recommended in humans. The herpes zoster (shingles), varicella, and yellow fever vaccines are live attenuated.

(Choice E) Toxoid (prepared from formalin- or heat-treated toxin) can induce humoral immunity against the corresponding toxin without producing serious toxic effects. However, rabies does not appear predominantly toxin-mediated. The tetanus-(reduced) diphtheria vaccine contains inactivated bacterial toxoids.

Educational objective:
In the United States, bats are the main source of rabies (only transmitted by mammals). Agitation and spasms progressing to coma within weeks of exposure is strongly suggestive of rabies encephalitis. Prophylactic vaccination is recommended for individuals at high risk for exposure to rabid animals or their tissues. The approved rabies vaccines consist of various rhabdovirus strains grown in tissue cell culture and then inactivated.

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A 43-year-old man comes to the emergency department due to 2 weeks of intermittent fevers, malaise, and headaches. He has a history of HIV and has not been taking his antiretroviral drugs recently. Five years ago, the patient spent a year in jail. Temperature is 38.2 C (100.8 F). Cerebrospinal fluid (CSF) analysis shows markedly elevated protein and low glucose, and CSF cultures grow *Mycobacterium tuberculosis*. Resistance testing shows the following:

Rifampin	sensitive
Isoniazid	sensitive
Pyrazinamide	sensitive
Ethambutol	sensitive
Streptomycin	resistant
Moxifloxacin	sensitive

Which of the following best explains the resistance pattern seen in these bacteria?

A. Altered structure of bacterial ribosomal proteins

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Pyrazinamide	sensitive
Ethambutol	sensitive
Streptomycin	resistant
Moxifloxacin	sensitive

Which of the following best explains the resistance pattern seen in these bacteria?

A. Altered structure of bacterial ribosomal proteins
B. Altered structure of enzymes involved in DNA winding-unwinding
C. Altered structure of enzymes involved in RNA synthesis
D. Decreased activity of bacterial catalase-peroxidase
E. Increased activity of enzymes involved in cell wall polysaccharide synthesis

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Pyrazinamide	sensitive
Ethambutol	sensitive
Streptomycin	resistant
Moxifloxacin	sensitive

Which of the following best explains the resistance pattern seen in these bacteria?

- A. Altered structure of bacterial ribosomal proteins (74%)
- B. ~~Altered structure of enzymes involved in DNA winding-unwinding~~ (3%)
- C. ~~Altered structure of enzymes involved in RNA synthesis~~ (10%)
- D. Decreased activity of bacterial catalase-peroxidase (3%)
- E. Increased activity of enzymes involved in cell wall polysaccharide synthesis (8%)

Correct

74%

01 min, 12 secs

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Drugs for treatment of tuberculosis		
Drug	**Mechanism of action**	**Side effects**
(R)ifampin	Inhibition of bacterial DNA-dependent RNA polymerase	GI side effects, rash, red-orange body fluids, cytopenias
(I)soniazid	Inhibition of mycolic acid synthesis	Neurotoxicity (give vitamin B_6/pyridoxine), hepatotoxicity
(P)yrazinamide	Unclear	Hepatotoxicity, hyperuricemia
(E)thambutol	Inhibition of arabinosyl transferase (?)	Optic neuropathy

GI = gastrointestinal.

This patient with HIV has fever, headache, and central nervous system (eg, spinal fluid) culture growing ***Mycobacterium tuberculosis***, consistent with *M tuberculosis* meningitis. Initial management is best accomplished through combination therapy with isoniazid (INH), rifampin, pyrazinamide, and either an

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This patient with HIV has fever, headache, and central nervous system (eg, spinal fluid) culture growing ***Mycobacterium tuberculosis***, consistent with *M tuberculosis* meningitis. Initial management is best accomplished through combination therapy with isoniazid (INH), rifampin, pyrazinamide, and either an injectable aminoglycoside or a fluoroquinolone.

Streptomycin is one of the older drugs in the aminoglycoside family; therefore, bacterial resistance to this antibiotic is widespread, resulting in its current usage being limited mainly to the treatment of tuberculosis, plague, and tularemia. Like other aminoglycosides, streptomycin can be administered only parenterally. It works by interfering with the 16s rRNA of the bacterial **30S ribosomal subunit**, thereby preventing bacterial protein synthesis. Mutations of the genes that encode ribosomal proteins are responsible for aminoglycoside resistance because they lead to modifications in the ribosomal binding sites for these drugs. Other resistance mechanisms to aminoglycosides include aminoglycoside-modifying enzymes (eg, transferases) and mutated porins.

(Choice B) Structural alteration of enzymes involved in DNA winding-unwinding is the means by which many microorganisms become resistant to fluoroquinolone antibiotics. Fluoroquinolones inhibit the bacterial enzymes DNA gyrase (topoisomerase II) and topoisomerase IV.

(Choice C) Structural alteration of enzymes involved in RNA synthesis is the mechanism through which

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bacterial enzymes DNA gyrase (topoisomerase II) and topoisomerase IV.

(Choice C) Structural alteration of enzymes involved in RNA synthesis is the mechanism through which organisms become resistant to rifampin. Rifampin inhibits the bacterial DNA-dependent RNA polymerase, thereby preventing the transcription of DNA into mRNA.

(Choice D) Decreased activity of bacterial catalase-peroxidase is a mechanism of mycobacterial resistance to INH. Mycobacterial catalase-peroxidase is required for the initial enzymatic conversion of INH to its active metabolite within the mycobacterial cells; without this enzyme, INH is unable to inhibit mycobacterial mycolic acid synthesis.

(Choice E) Increased activity of enzymes involved in cell wall polysaccharide synthesis is the means by which mycobacteria develop resistance to ethambutol. Ethambutol interferes specifically with mycobacterial peptidoglycan cell wall synthesis, possibly through inhibition of arabinosyl transferase. This drug is ineffective against organisms other than mycobacteria.

Educational objective:

- The aminoglycoside streptomycin inhibits protein synthesis by inactivating the 30S (small) ribosomal subunit.

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resistance to INH. Mycobacterial catalase-peroxidase is required for the initial enzymatic conversion of INH to its active metabolite within the mycobacterial cells; without this enzyme, INH is unable to inhibit mycobacterial mycolic acid synthesis.

(Choice E) Increased activity of enzymes involved in cell wall polysaccharide synthesis is the means by which mycobacteria develop resistance to ethambutol. Ethambutol interferes specifically with mycobacterial peptidoglycan cell wall synthesis, possibly through inhibition of arabinosyl transferase. This drug is ineffective against organisms other than mycobacteria.

Educational objective:

- The aminoglycoside streptomycin inhibits protein synthesis by inactivating the 30S (small) ribosomal subunit.
- Decreased activity of bacterial catalase-peroxidase is a mechanism of mycobacterial resistance to isoniazid.
- Structural alteration of enzymes involved in RNA synthesis (DNA-dependent RNA polymerase) is the mechanism through which organisms become resistant to rifampin.

Microbiology	Infectious Diseases	Antibiotic resistance
Subject	System	Topic

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A 13-year-old boy with cystic fibrosis comes to the clinic with a persistent cough over the past 2 weeks despite treatment with several oral antibiotics. Temperature is 36.7 C (98.1 F). Pulmonary examination reveals diffuse wheezing. Pulmonary function testing is consistent with an exacerbation of the underlying disease, and the patient is admitted for broad-spectrum intravenous antibiotics and aggressive respiratory therapy. Induced sputum is collected for cultures. In addition to blood, chocolate, and MacConkey agar, this patient's sputum should also be cultured on which of the following media?

A. *Bordetella pertussis*–selective agar
B. *Burkholderia cepacia*–selective agar
C. *Corynebacterium* species–specific agar
D. *Legionella pneumophila*–selective agar
E. *Salmonella-Shigella* agar

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A. *Bordetella pertussis*–selective agar (23%)
✓ B. *Burkholderia cepacia*–selective agar (37%)
C. *Corynebacterium* species–specific agar (5%)
D. *Legionella pneumophila*–selective agar (28%)
E. *Salmonella-Shigella* agar (4%)

Correct

37%
Answered correctly

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Features of cystic fibrosis	
Pathogenesis	• Autosomal recessive mutation (Δ**F508**) impairs CFTR function • Decreased water content causes **thick, viscous mucus**: ◦ Chronic airway obstruction ◦ Gastrointestinal malabsorption
Clinical manifestations	• Chronic, productive cough • Recurrent **sinopulmonary infections** (eg, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, & *Burkholderia cepacia* complex) • **Pancreatic insufficiency** • Male infertility (bilateral absence of vas deferens)
Diagnosis	• Elevated sweat chloride levels • Nasal potential difference measurements • Genetic testing for *CFTR* mutations

CFTR = cystic fibrosis transmembrane conductance regulator.

Cystic fibrosis (CF) is an autosomal recessive disorder in which an abnormality in the CF transmembrane

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Cystic fibrosis (CF) is an autosomal recessive disorder in which an abnormality in the CF transmembrane conductance regulator results in the accumulation of thick, viscous mucus in multiple organ systems. In particular, inspissated airway secretions block the respiratory tract and impair mucociliary clearance, leading to bacterial colonization and chronic, recurrent sinopulmonary infections.

CF **pulmonary exacerbations** are characterized by a decline in lung function (ie, forced expiratory volume in 1 sec) and new or worsening cough, shortness of breath, or sputum production. Infection and subsequent airway inflammation are typically responsible for the acute change in respiratory status, and common bacterial pathogens include ***Staphylococcus aureus***, nontypeable ***Haemophilus influenzae***, and ***Pseudomonas aeruginosa***. With progressive disease, however, patients are also at risk for colonization with ***Burkholderia cepacia* complex**, a fastidious gram-negative bacterium that is often difficult to eradicate and associated with increased morbidity and mortality.

Sputum cultures are typically performed during CF pulmonary exacerbation to identify the pathogen and guide antimicrobial management. In addition to regular blood (eg, *Streptococcus*), chocolate (eg, *H influenzae*), and MacConkey (eg, *Pseudomonas*) agars, sputum should also be plated on mannitol salt agar (eg, *S aureus*) and *B cepacia*–selective agar.

(Choices A, C, D, and E) *Bordetella pertussis*, *Corynebacterium*, *Legionella*, *Salmonella*, and *Shigella* do not commonly cause CF exacerbations.

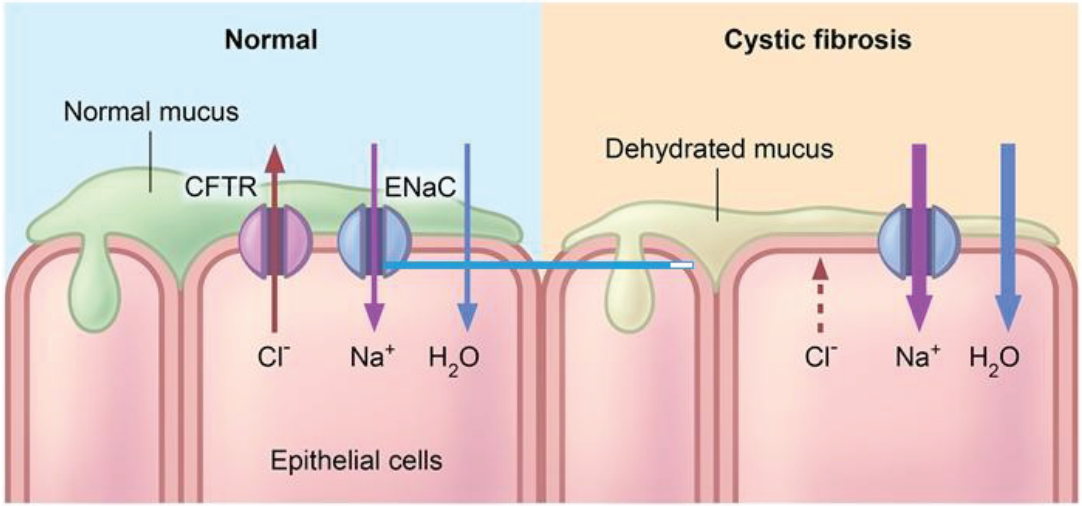
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Cystic fibrosis (CF) is an autosomal recessive disorder in which an abnormality in the CF transmembrane

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Respiratory mucosa



CFTR = cystic fibrosis transmembrane conductance regulator; **ENaC** = epithelial sodium channel.

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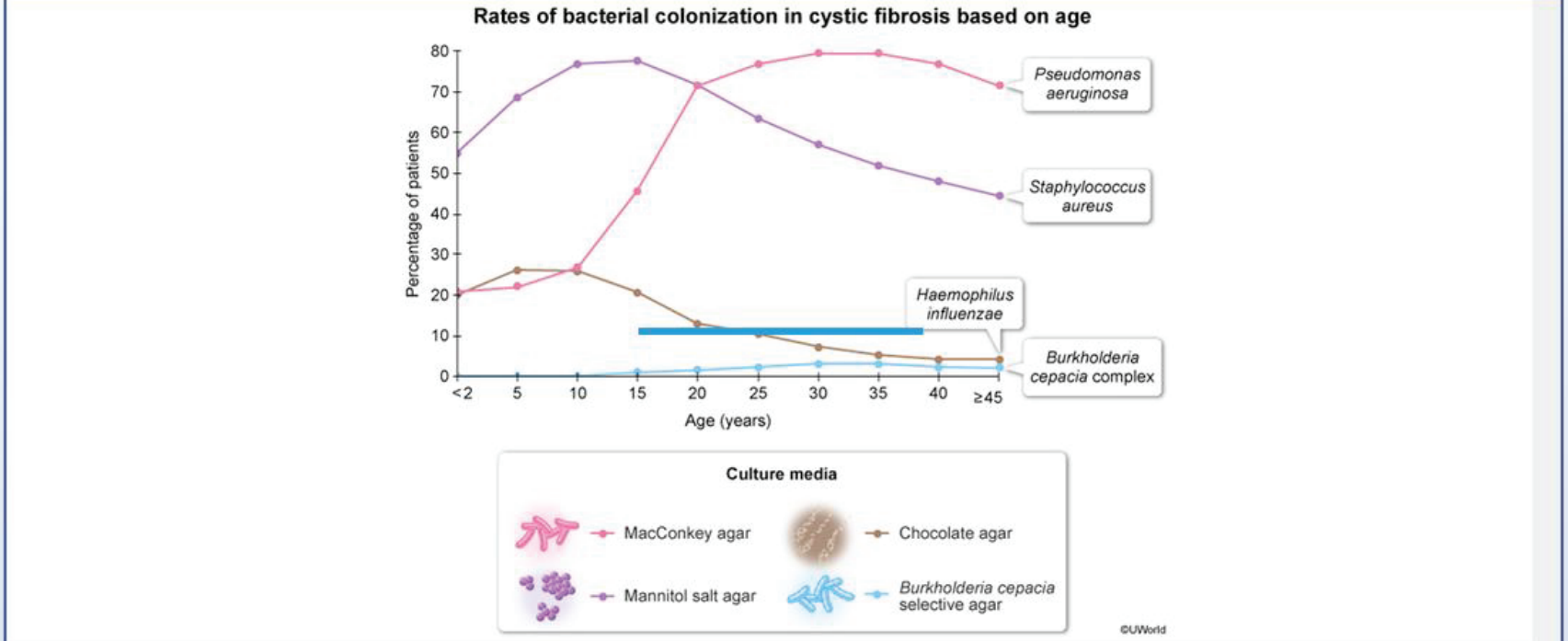
not commonly cause CF exacerbations

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Cystic fibrosis (CF) is an autosomal recessive disorder in which an abnormality in the CF transmembrane

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not commonly cause CF exacerbations

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(Choices A, C, D, and E) *Bordetella pertussis*, *Corynebacterium*, *Legionella*, *Salmonella*, and *Shigella* do not commonly cause CF exacerbations.

Educational objective:

Patients with cystic fibrosis are at risk for pulmonary exacerbations due to *Staphylococcus aureus*, *Pseudomonas aeruginosa*, nontypeable *Haemophilus influenzae*, and *Burkholderia cepacia* complex.

References

- Antibiotic treatment for Burkholderia cepacia complex in people with cystic fibrosis experiencing a pulmonary exacerbation.

Microbiology	Infectious Diseases	Cystic fibrosis
Subject	System	Topic

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The following vignette applies to the next **2** items. The items in the set must be answered in sequential order. Once you click **Proceed to Next Item**, you will not be able to add or change an answer.

An isolate of *Streptococcus pneumoniae* from a patient with meningitis is incubated with low-dose radiolabeled ceftriaxone and then subjected to protein electrophoresis. Five distinct bands are detected by radioautography.

Item 1 of 2

These bands most likely represent radiolabeled ceftriaxone that is bound to which of the following?

A. Cell wall glycoproteins
B. DNA replication proteins
C. Porins
D. Ribosomal proteins
E. Transpeptidases

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An isolate of *Streptococcus pneumoniae* from a patient with meningitis is incubated with low-dose radiolabeled ceftriaxone and then subjected to protein electrophoresis. Five distinct bands are detected by radioautography.

Item 1 of 2

These bands most likely represent radiolabeled ceftriaxone that is bound to which of the following?

A. Cell wall glycoproteins (50%)
B. DNA replication proteins (3%)
C. Porins (1%)
D. Ribosomal proteins (6%)
✓ E. Transpeptidases (38%)

Correct

38%
25 secs
10/25/2020

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Penicillins and cephalosporins function by **irreversibly** binding to penicillin-binding proteins. Transpeptidases are one form of penicillin-binding protein that function to cross-link peptidoglycan in the bacterial cell wall. Inhibition of transpeptidase (which occurs with the use of the cephalosporin ceftriaxone) leads to cell wall instability and bacteriolysis. Many bacterial species synthesize multiple different penicillin-binding proteins; the laboratory study described in this question stem identifies 5 such proteins that are produced by this isolate of *Streptococcus pneumoniae*.

(Choice A) Vancomycin binds to the terminal D-alanine residues of cell wall glycoproteins and prevents transpeptidases from forming cross-links.

(Choice B) Fluoroquinolones interfere with DNA replication by binding to proteins such as DNA gyrase.

(Choice C) Porins are utilized by bacterial organisms as a means of controlling diffusion of small to medium-sized metabolites. Antibiotic resistance can develop through porin mutations that prevent antibiotic diffusion through the outer membrane of gram-negative bacteria. No known antibiotics function by binding to porins.

(Choice D) Ribosomal proteins are bound by multiple antibiotics including macrolides, tetracyclines, and others.

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transpeptidases from forming cross-links.

(Choice B) Fluoroquinolones interfere with DNA replication by binding to proteins such as DNA gyrase.

(Choice C) Porins are utilized by bacterial organisms as a means of controlling diffusion of small to medium-sized metabolites. Antibiotic resistance can develop through porin mutations that prevent antibiotic diffusion through the outer membrane of gram-negative bacteria. No known antibiotics function by binding to porins.

(Choice D) Ribosomal proteins are bound by multiple antibiotics including macrolides, tetracyclines, and others.

Educational objective:
Penicillins and cephalosporins function by irreversibly binding to penicillin-binding proteins such as transpeptidases.

Microbiology	Infectious Diseases	Cephalosporins
Subject	System	Topic

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Item 2 of 2

Another isolate of *Streptococcus pneumoniae* from a patient with meningitis is also incubated with low-dose radioactive ceftriaxone and subjected to protein electrophoresis. Only two bands are detected using radioautography. Which of the following best explains the observed finding?

A. Action of beta-lactamases
B. Change in protein structure
C. Salvage metabolic pathway
D. Transmembranous efflux pumps
E. Upregulation of protein synthesis

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Item 2 of 2

Another isolate of *Streptococcus pneumoniae* from a patient with meningitis is also incubated with low-dose radioactive ceftriaxone and subjected to protein electrophoresis. Only two bands are detected using radioautography. Which of the following best explains the observed finding?

A. ~~Action of beta-lactamases~~ (37%)
B. Change in protein structure (52%)
C. ~~Salvage metabolic pathway~~ (0%)
D. ~~Transmembranous efflux pumps~~ (7%)
E. Upregulation of protein synthesis (1%)

Correct

52%
Answered correctly

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The isolate of *S. pneumoniae* in the prior question had five penicillin-binding proteins identified, whereas the isolate in the current question only has two. This indicates that three of the penicillin-binding proteins have been altered in such a way that inhibits the binding of ceftriaxone. Structural changes in penicillin-binding proteins that prevent ceftriaxone from binding is one mechanism for ceftriaxone resistance.

(Choice A) Beta-lactamases function to degrade penicillin and cephalosporins. Production of a beta-lactamase would prevent ceftriaxone from being able to bind to the penicillin-binding proteins. Because ceftriaxone is so much smaller than the penicillin-binding proteins, unbound ceftriaxone would likely accumulate at one of the electrodes. This would lead to no bands being found within the electrophoresis area.

(Choice C) A salvage metabolic pathway can restore metabolic function that would otherwise be inhibited by an antibiotic such as trimethoprim or sulfamethoxazole.

(Choice D) Transmembranous efflux pumps confer resistance to antibiotics that require entry into the cell to function (e.g., tetracyclines and macrolides). However, penicillins and cephalosporins function outside of the bacterial cell at the peptidoglycan cell wall.

(Choice E) Upregulation of protein synthesis can occur to overcome the effect of an antibiotic that binds to and irreversibly inhibits the action of that protein. However, if this were the mechanism for resistance, five

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(Choice C) A salvage metabolic pathway can restore metabolic function that would otherwise be inhibited by an antibiotic such as trimethoprim or sulfamethoxazole.

(Choice D) Transmembranous efflux pumps confer resistance to antibiotics that require entry into the cell to function (e.g., tetracyclines and macrolides). However, penicillins and cephalosporins function outside of the bacterial cell at the peptidoglycan cell wall.

(Choice E) Upregulation of protein synthesis can occur to overcome the effect of an antibiotic that binds to and irreversibly inhibits the action of that protein. However, if this were the mechanism for resistance, five bands would still be identified on the radioautography test.

Educational objective:
A change in the structure of penicillin-binding proteins that prevents cephalosporin binding is one mechanism of bacterial resistance to cephalosporins.

Microbiology	Infectious Diseases	Antibiotic resistance
Subject	System	Topic

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A 36-year-old man is admitted to the hospital with severe left leg pain after suffering a minor laceration to his leg 2 days earlier. His temperature is 39.5 C (103 F) and blood pressure is 85/45 mm Hg. On physical examination, the patient's left leg is swollen and firm with erythema of the overlying skin. There is a small wound draining blood-tinged exudate on his left calf. The patient is taken to the operating room immediately and a large area of necrotic tissue is excised. Gram stain of the necrotic tissue shows Gram-positive cocci and culture of the bacteria performed on a blood agar plate grows small colonies with a wide zone of surrounding hemolysis. Coagulase and catalase tests are negative and pyrrolidonyl arylamidase (PYR) test is positive. Which of the following pathogens is most likely responsible for this patient's condition?

A. *Aeromonas hydrophila*
B. *Clostridium perfringens*
C. *Staphylococcus aureus*
D. *Streptococcus agalactiae*
E. *Streptococcus pyogenes*

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examination, the patient's left leg is swollen and firm with erythema of the overlying skin. There is a small wound draining blood-tinged exudate on his left calf. The patient is taken to the operating room immediately and a large area of necrotic tissue is excised. Gram stain of the necrotic tissue shows Gram-positive cocci and culture of the bacteria performed on a blood agar plate grows small colonies with a wide zone of surrounding hemolysis. Coagulase and catalase tests are negative and pyrrolidonyl arylamidase (PYR) test is positive. Which of the following pathogens is most likely responsible for this patient's condition?

A. *Aeromonas hydrophila* (1%)
B. *Clostridium perfringens* (19%)
C. *Staphylococcus aureus* (2%)
D. *Streptococcus agalactiae* (6%)
✓ E. *Streptococcus pyogenes* (70%)

Correct
70%
02 mins, 01 sec
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Features of necrotizing fasciitis	
Microbiology	• *Streptococcus pyogenes* (group A streptococci) • *Staphylococcus aureus* • *Clostridium perfringens* • Polymicrobial
Pathogenesis	• Bacteria spread rapidly through subcutaneous tissue & deep fascia, undermining the skin • Most commonly involves extremities & perineal region
Clinical manifestations	• Often antecedent history of minor trauma • Erythema of overlying skin • Swelling & edema • Pain **out of proportion** to examination findings • Systemic symptoms (eg, **fever & hypotension**)
Treatment	• Requires **surgical debridement** & broad-spectrum antibiotics

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This patient has necrotizing fasciitis ("flesh-eating disease"), a severe soft-tissue infection characterized by fulminant tissue necrosis and high mortality. The microbiologic differential for this condition includes ***Streptococcus pyogenes, Staphylococcus aureus, Clostridium perfringens***, *Streptococcus agalactiae*, and *Aeromonas hydrophila*. Of these options, *S pyogenes* (group A strep) is the only Gram-positive cocci that is coagulase-negative, catalase-negative, and pyrrolidonyl arylamidase (PYR)-positive. It also forms small colonies with a wide zone of beta-hemolysis and is sensitive to bacitracin (which has been widely replaced by the PYR test).

S pyogenes can be transmitted through wounds and spreads rapidly to the deep layers of the skin and fascia due to production of hyaluronidase and other hydrolytic enzymes. M protein is another major virulence factor that allows the bacteria to evade phagocytosis by preventing activation of the alternate complement pathway. The bacterium also secretes a multitude of extracellular toxins, including hemolysins O and S (cytotoxins that cause hemolysis) and pyrogenic exotoxins (superantigens that result in tissue injury and septic shock).

Typically, there is a sudden onset of **severe pain** and swelling at a site of trauma or recent surgery. Patients quickly become **hypotensive** and develop septic shock. Necrotizing fasciitis is initially treated with **aggressive surgical debridement** of all necrotic tissue along with empiric broad-spectrum antibiotics

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Typically, there is a sudden onset of **severe pain** and swelling at a site of trauma or recent surgery. Patients quickly become **hypotensive** and develop septic shock. Necrotizing fasciitis is initially treated with **aggressive surgical debridement** of all necrotic tissue along with empiric broad-spectrum antibiotics due to the high incidence of polymicrobial infection.

(Choice A) *A hydrophila* is an oxidase-positive, non-lactose-fermenting, Gram-negative rod. It can cause gastroenteritis, wound infections, and bacteremia following exposure to contaminated water.

(Choice B) *C perfringens* is a large, spore-forming, anaerobic, Gram-positive rod that is catalase- and coagulase-negative. It is implicated in food poisoning, clostridial myonecrosis (gas gangrene), and bacteremia. On blood agar, it produces a double zone of beta-hemolysis.

(Choice C) *S aureus* is Gram-positive coccus that grows in clusters. It is catalase-positive, coagulase-positive, and PYR-negative. *S aureus* produces large colonies and demonstrates beta-hemolysis. Like *S pyogenes*, *S aureus* can also cause monomicrobial necrotizing fasciitis.

(Choice D) *S agalactiae* (group B strep) is a coagulase- and catalase-negative, Gram-positive cocci that grows in chains. Colonies produce a narrow zone of beta-hemolysis that enhances when plated perpendicular to *S aureus* (positive CAMP test). *S agalactiae* can cause skin and soft-tissue infections as well as **newborn sepsis and meningitis**.

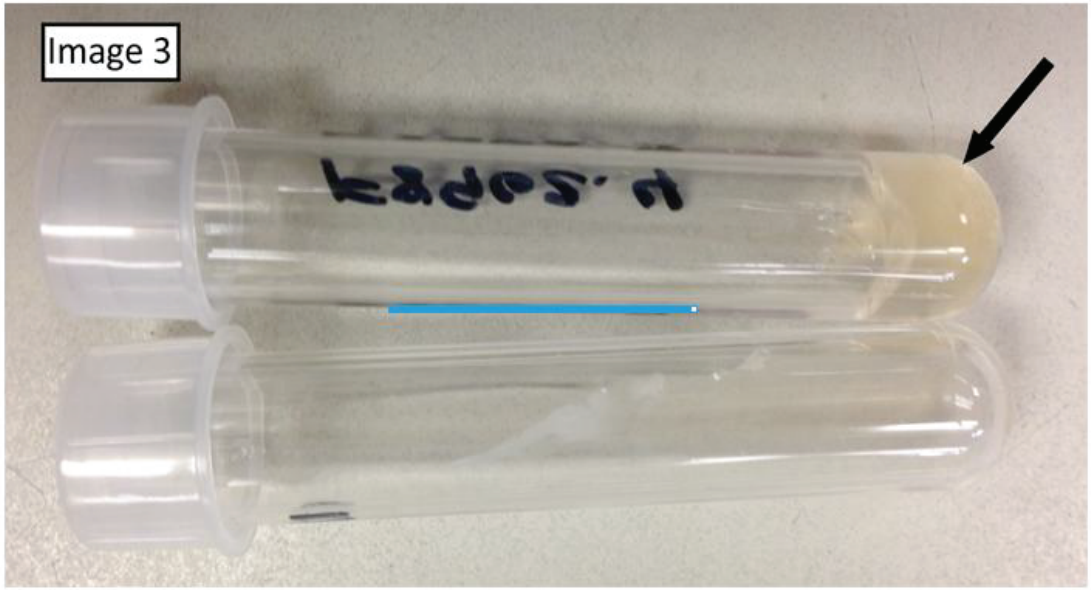
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Typically, there is a sudden onset of severe pain and swelling at a site of trauma or recent surgery.

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How do you treat this patient and investigate?

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bacteremia. On blood agar, it produces a double zone of beta-hemolysis.

(Choice C) *S aureus* is Gram-positive coccus that grows in clusters. It is catalase-positive, coagulase-positive, and PYR-negative. *S aureus* produces large colonies and demonstrates beta-hemolysis. Like *S pyogenes*, *S aureus* can also cause monomicrobial necrotizing fasciitis.

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Educational objective:
Necrotizing fasciitis is a severe infection of the subcutaneous tissue and deep fascia that is a surgical emergency. The infection is often polymicrobial, but monomicrobial cases due to *Streptococcus pyogenes* (group A strep) can also occur. *S pyogenes* is a **pyrrolidonyl arylamidase (PYR)-positive**, beta-hemolytic, Gram-positive cocci that grows in chains.

Microbiology	Infectious Diseases	Necrotizing soft tissue infections
Subject	System	Topic

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A 24-year-old woman comes to the emergency department due to joint pain. A week ago, the patient had a flu-like illness with fever, malaise, and fleeting joint aches in her wrists, ankles, and knees. Over the past 2 days, the joint pain worsened, and she developed new swelling of the right knee. The patient has no chronic medical problems and has had no similar symptoms in the past. She does not use tobacco, alcohol, or injection drugs. She is sexually active, uses an oral contraceptive for birth control, and her last menstrual period was a week ago. Temperature is 38 C (100.4 F). On examination, there is no scleral icterus, facial rash, or oral ulcers but a few scattered painless vesicopustular lesions are present on the upper extremities. The right knee is warm, swollen, and tender with decreased range of motion. Both ankles and the left wrist are mildly tender to palpation but not swollen or erythematous. Arthrocentesis of the right knee joint yields 20 mL of cloudy fluid with a leukocyte count of 50,000/mm^3 (90% neutrophils). Additional evaluation of the joint fluid is most likely to show which of the following in this patient?

A. Gram-negative intracellular diplococci

B. Gram-negative oxidase-negative curved rods

C. Gram-positive alpha-hemolytic cocci in chains

D. Gram-positive catalase-positive cocci in clusters

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A. Gram-negative intracellular diplococci
B. Gram-negative oxidase-negative curved rods
C. Gram-positive alpha-hemolytic cocci in chains
D. Gram-positive catalase-positive cocci in clusters
E. Needle-shaped negatively birefringent crystals
F. Rhomboid-shaped positively birefringent crystals

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menstrual period was a week ago. Temperature is 38 C (100.4 F). On examination, there is no scleral icterus, facial rash, or oral ulcers but a few scattered painless vesicopustular lesions are present on the upper extremities. The right knee is warm, swollen, and tender with decreased range of motion. Both ankles and the left wrist are mildly tender to palpation but not swollen or erythematous. Arthrocentesis of the right knee joint yields 20 mL of cloudy fluid with a leukocyte count of 50,000/mm^3 (90% neutrophils). Additional evaluation of the joint fluid is most likely to show which of the following in this patient?

- A. Gram-negative intracellular diplococci (69%)
- B. ~~Gram-negative oxidase-negative curved rods~~ (3%)
- C. ~~Gram-positive alpha-hemolytic cocci in chains~~ (4%)
- D. Gram-positive catalase-positive cocci in clusters (19%)
- E. ~~Needle-shaped negatively birefringent crystals~~ (1%)
- F. ~~Rhomboid-shaped positively birefringent crystals~~ (1%)

Correct

69%
Answered correctly

03 mins, 26 secs
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Last Updated

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This patient has purulent arthritis of the knee, oligoarticular joint pain, and a few vesiculopustular lesions on the extremities, raising suspicion for **disseminated gonococcal infection** (DGI). DGI is one of the most common causes of **septic arthritis** in young, sexually active individuals. It is due to the spread of ***Neisseria gonorrhoeae*** from a (usually asymptomatic) genitourinary infection into the systemic circulation. Patients typically present with either purulent arthritis or the triad of polyarthralgia, dermatitis, and tenosynovitis; however, some overlap in these 2 syndromes can occur (as in this patient). The diagnosis is made when blood, urine, or joint fluid microscopy and culture reveal gram-negative intracellular diplococci.

(Choice B) Salmonella appears as a gram-negative oxidase-negative curved rod. Patients with sickle cell disease are at increased risk of septic arthritis due to salmonella. However, salmonella is an uncommon cause of septic arthritis in patients who do not have sickle cell disease.

(Choice C) Viridans streptococci, a gram-positive alpha-hemolytic cocci in chains, is a common cause of infective endocarditis and can lead to septic arthritis (due to septic emboli). Patients with infective endocarditis can have flu-like symptoms and skin findings (eg, Osler nodes, Janeway lesions). However, vesiculopustular lesions on the arms are much more characteristic of DGI.

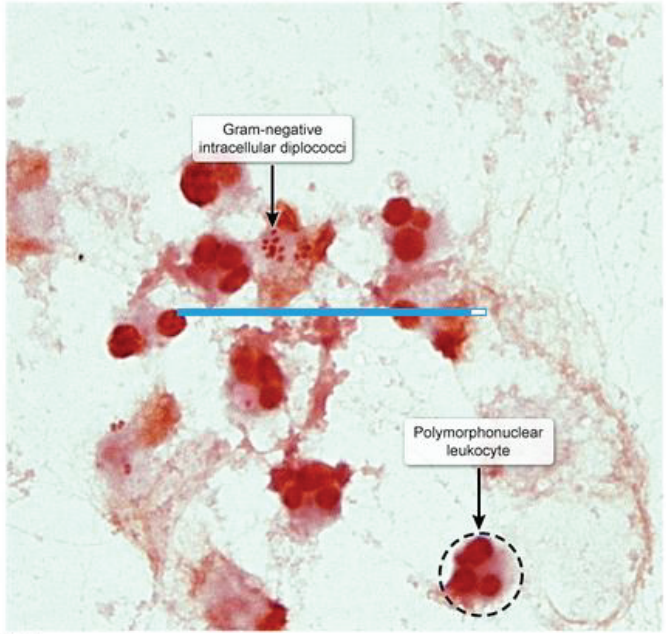
(Choice D) *Staphylococcus aureus*, a catalase-positive gram-positive cocci in clusters, is the most

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Neisseria gonorrhoeae



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(Choice D) Staphylococcus aureus, a catalase-positive gram-positive cocci in clusters, is the most

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(Choice D) *Staphylococcus aureus*, a catalase-positive gram-positive cocci in clusters, is the most common cause of septic arthritis. However, most cases in young adults are linked to injection drug use. In addition, the presence of vesiculopustular lesions and oligoarticular arthralgias make gonococcal arthritis more likely.

(Choices E and F) Gout is caused by monosodium urate crystals that appear as needle-shaped negatively bifringent crystals. Pseudogout is caused by calcium pyrophosphate dihydrate crystals that appear as rhomboid-shaped positively bifringent crystals. Both gout and pseudogout cause inflammatory arthritis (eg, redness, warmth, pain, disability) with elevated leukocyte counts on joint fluid aspiration. However, migrating arthralgias and vesiculopustular lesions would be atypical.

Educational objective:

Septic arthritis in a young, sexually active adult should raise suspicion for disseminated *Neisseria gonorrhoeae* infection. Patients may also have the triad of polyarthritis, a vesiculopustular skin rash, and tenosynovitis. *N gonorrhoeae* is a gram-negative diplococci that is usually identified by microscopy, culture, or nucleic acid amplification.

References

- Gonococcal arthritis (disseminated gonococcal infection).

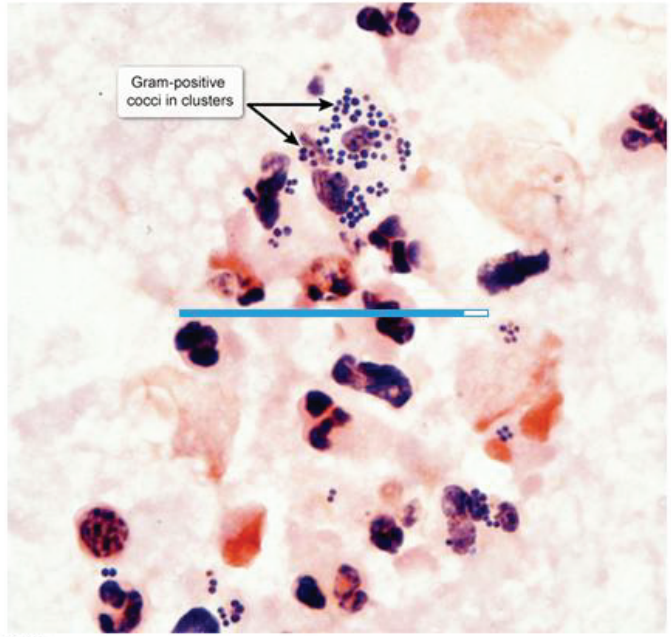
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(Choice D) *Staphylococcus aureus*, a catalase-positive gram-positive cocci in clusters, is the most

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Staphylococcus aureus



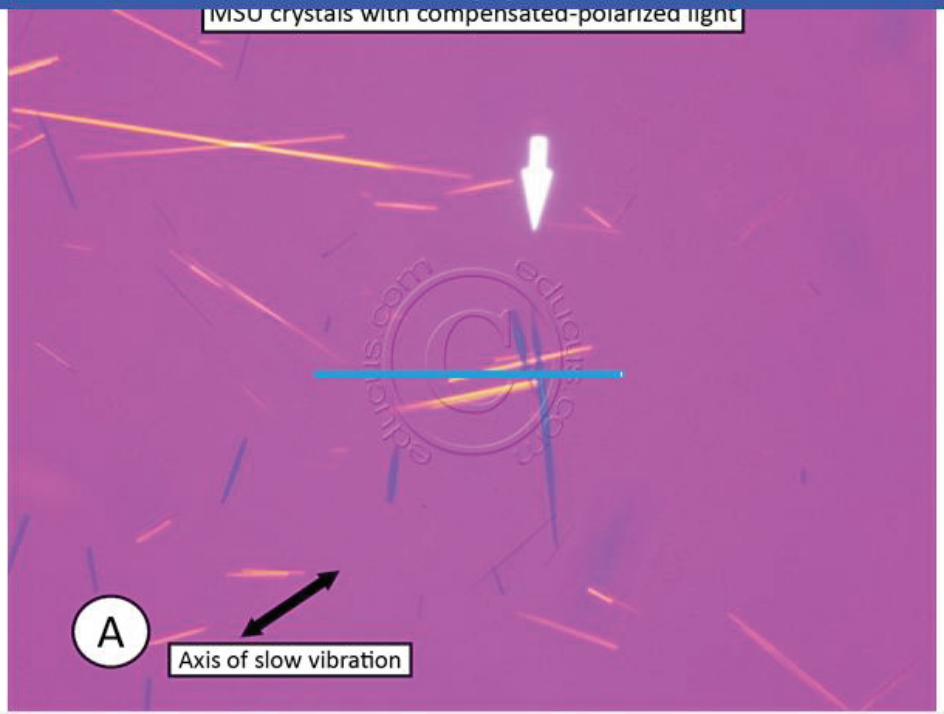
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(Choice D) *Staphylococcus aureus*, a catalase-positive gram-positive cocci in clusters, is the most

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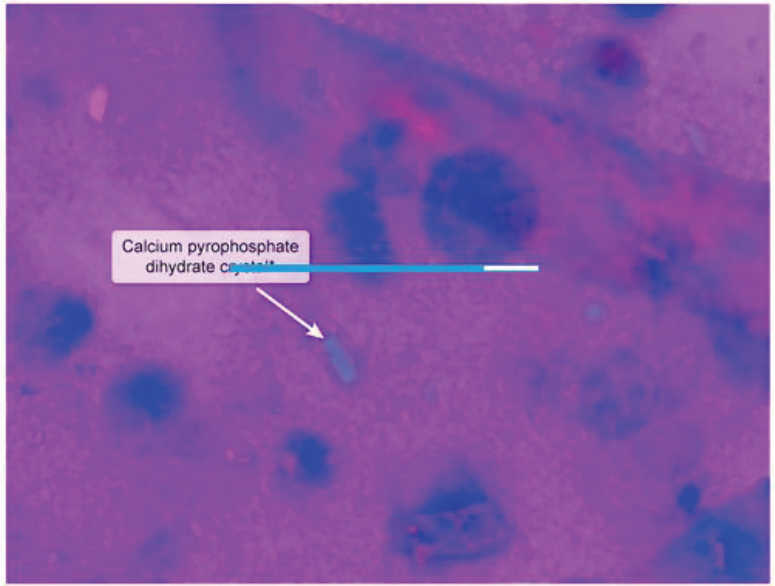
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(Choice D) *Staphylococcus aureus*, a catalase-positive gram-positive cocci in clusters, is the most

Exhibit Display

Synovial fluid with CPPD crystals Synovial fluid with calcium pyrophosphate dihydrat

Pseudogout



*Rhomboid-shaped, positively birefringent crystal under compensated polarized light ©UWorld

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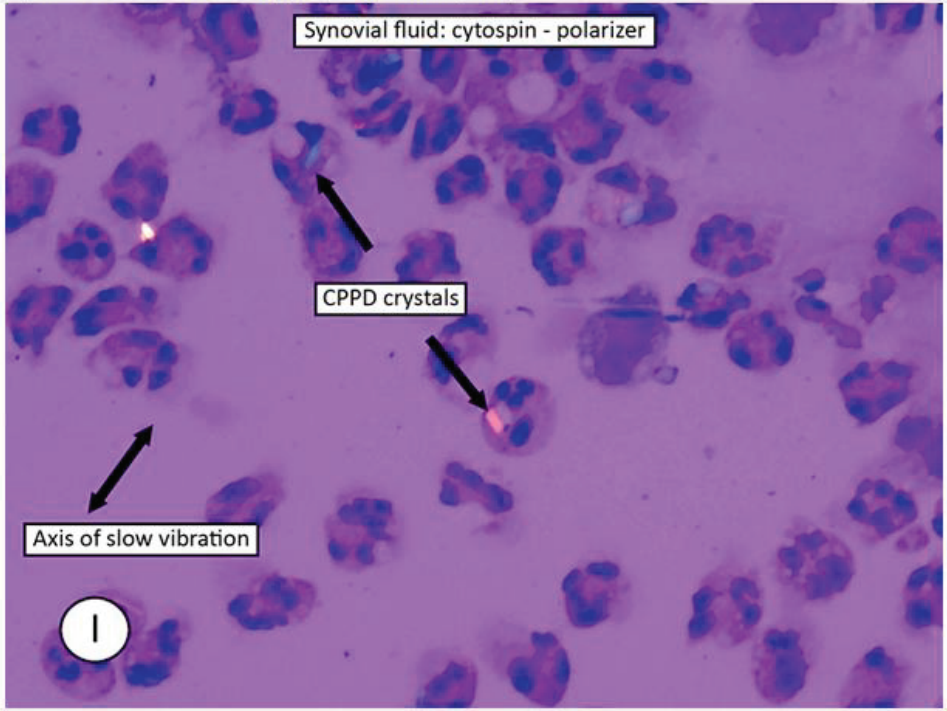
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(Choice D) *Staphylococcus aureus*, a catalase-positive gram-positive cocci in clusters, is the most

Exhibit Display

Synovial fluid with CPPD crystals | Synovial fluid with calcium pyrophosphate dihydrat



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A 45-year-old man comes to the office with groin pain and swelling. About a month ago, he noticed a sore on his penis but did not seek medical attention because the ulcer was not painful and disappeared within a week. Several days ago, he began to experience painful swelling in his inguinal region, with inflammation of the overlying skin and eventual formation of several draining ulcers. He also has mild fever and malaise that began around the same time as his groin symptoms. The patient is a sailor. His other medical problems include well-controlled hypertension and hyperlipidemia. Cell scrapings from his lesions show cytoplasmic inclusion bodies. Which of the following is the most likely cause of this patient's condition?

A. *Chlamydia trachomatis*
B. *Haemophilus ducreyi*
C. Herpes simplex virus
D. *Klebsiella granulomatis*
E. *Treponema pallidum*

Submit

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- A. *Chlamydia trachomatis* (42%)
- B. ~~*Haemophilus ducreyi*~~ (12%)
- C. ~~Herpes simplex virus~~ (9%)
- D. *Klebsiella granulomatis* (6%)
- E. ~~*Treponema pallidum*~~ (28%)

42% 01 min, 37 secs 01/16/2021

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Characteristics of ulcerative sexually transmitted diseases			
Disease	**Causative agent**	**Features of primary lesion**	**Initial lesion painful?**
Chancroid	*Haemophilus ducreyi*	• Multiple & deep ulcers • Base may have gray to yellow exudate • Organisms often clump in long parallel strands ("school of fish")	Yes
Genital herpes	Herpes simplex virus 1 & 2	• Multiple, small, grouped ulcers • Shallow with erythematous base • Multinucleated giant cells & intranuclear inclusions (Cowdry type A)	Yes
		• Extensive & progressive ulcerative	

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		A)	
Granuloma inguinale (donovanosis)	*Klebsiella granulomatis*	• Extensive & progressive ulcerative lesions without lymphadenopathy • Base may have granulation-like tissue • Deeply staining gram-negative intracytoplasmic cysts (Donovan bodies)	No
Syphilis	*Treponema pallidum*	• Single, indurated, well-circumscribed ulcer • Nonexudative base • Painless inguinal lymphadenopathy • Thin, delicate, corkscrew-shaped organisms on dark-field microscopy	No
Lymphogranuloma	*Chlamydia*	• Small & shallow ulcers • Large, painful, coalesced inguinal	

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Lymphogranuloma venereum	*Chlamydia trachomatis*	• Small & shallow ulcers • Large, painful, coalesced inguinal lymph nodes ("buboes") • Intracytoplasmic chlamydial inclusion bodies in epithelial cells & leukocytes	No

Chlamydia trachomatis is a small, gram-negative (albeit difficult to stain), obligate **intracellular** bacterium. Serotypes A through C cause ocular infection (trachoma) in children; serotypes D through K cause urogenital (sexually transmitted) infections and inclusion conjunctivitis; and serotypes L1 through L3 cause **lymphogranuloma venereum** (LGV).

LGV is characterized initially by a painless, small, shallow genital ulcer containing infected cells. The **painless** nature helps distinguish LGV from other diseases. The appearance of the ulcer is followed weeks later by swollen, **painful**, coalescing **inguinal nodes** (**"buboes"**) that can develop stellate abscesses and rupture. If left untreated, LGV can cause fibrosis, lymphatic obstruction, and anogenital strictures and fistulas. Histologically, LGV lesions contain areas of mixed granulomatous and neutrophilic inflammation with **intracytoplasmic chlamydial inclusion bodies** in epithelial and inflammatory cells.

Doxycycline is recommended. Although it is relatively uncommon in the United States or Western Europe

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Doxycycline is recommended. Although it is relatively uncommon in the United States or Western Europe, LGV is endemic in some parts of the world.

(Choice B) *Haemophilus ducreyi* causes chancroid, an ulcerative, sexually transmitted infection characterized by **painful** (rather than painless) red papules on the genitals that eventually erode to become tender ulcers (you "do cry" with *H ducreyi*). Regional lymph nodes may swell and become chronic ulcers.

(Choice C) Herpes simplex virus type 2 is the most common cause of genital herpes, characterized by vesicles that develop into shallow ulcers. These lesions are often painful and heal within 10 days. Histologically, multinucleated giant cells and large pinkish-purple intranuclear (not intracytoplasmic) inclusions, termed Cowdry type A bodies, are present.

(Choice D) *Klebsiella granulomatis* causes granuloma inguinale (donovanosis), which also initially manifests as a painless genital papule that eventually ulcerates; however, lymphadenopathy is uncommon. Intracytoplasmic Donovan bodies are diagnostic. If donovanosis is untreated, scarring and strictures can lead to severe lymphatic obstruction and lymphedema (elephantiasis).

(Choice E) Syphilis, caused by the gram-negative spirochete *Treponema pallidum,* is initially characterized by a painless lesion (chancre) that heals without treatment within weeks. It does not typically develop into buboes and is not characterized by cytoplasmic inclusion bodies.

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(Choice E) Syphilis, caused by the gram-negative spirochete *Treponema pallidum,* is initially characterized by a painless lesion (chancre) that heals without treatment within weeks. It does not typically develop into buboes and is not characterized by cytoplasmic inclusion bodies.

Educational objective:

Chlamydia trachomatis serotypes L1 through L3 cause lymphogranuloma venereum, a sexually transmitted disease characterized initially by painless ulcers with later progression to painful inguinal lymphadenopathy ("buboes") and ulceration. Chlamydial inclusion bodies are seen in host cell cytoplasm.

References

- Prevention and treatment of sexually transmitted diseases: an update.

Microbiology	Infectious Diseases	Lymphogranuloma venerum
Subject	System	Topic

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A 46-year-old man comes to the emergency department due to fever. He returned from a vacation in Southeast Asia a week ago and began having symptoms toward the end of his trip. The patient describes continuous fever that has risen slowly to reach a high plateau and is relieved only by antipyretics. He has also had headaches and abdominal discomfort; he initially had constipation but has had loose stools for the past several days. Temperature is 40 C (104 F), blood pressure is 114/68 mm Hg, and pulse is 62/min. No oropharyngeal lesions, cervical lymphadenopathy, or neck rigidity is present. Lungs are clear on auscultation, and heart sounds are normal. Abdominal examination shows mild distension and generalized tenderness with hepatosplenomegaly. There is a faint, erythematous, macular skin rash over the trunk and abdomen. Laboratory studies reveal mild, normocytic, normochromic anemia and leukopenia with left shift. Peripheral blood smear is normal. Which of the following is the most likely route of transmission of this patient's infection?

A. Bite from a vector insect
B. Exposure to a carrier animal
C. Ingestion of contaminated food
D. Inhalation of infectious droplets

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past several days. Temperature is 40 C (104 F), blood pressure is 114/68 mm Hg, and pulse is 62/min. No oropharyngeal lesions, cervical lymphadenopathy, or neck rigidity is present. Lungs are clear on auscultation, and heart sounds are normal. Abdominal examination shows mild distension and generalized tenderness with hepatosplenomegaly. There is a faint, erythematous, macular skin rash over the trunk and abdomen. Laboratory studies reveal mild, normocytic, normochromic anemia and leukopenia with left shift. Peripheral blood smear is normal. Which of the following is the most likely route of transmission of this patient's infection?

A. Bite from a vector insect
B. Exposure to a carrier animal
C. Ingestion of contaminated food
D. Inhalation of infectious droplets
E. Sexual contact with infected person

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past several days. Temperature is 40 C (104 F), blood pressure is 114/68 mm Hg, and pulse is 62/min. No oropharyngeal lesions, cervical lymphadenopathy, or neck rigidity is present. Lungs are clear on auscultation, and heart sounds are normal. Abdominal examination shows mild distension and generalized tenderness with hepatosplenomegaly. There is a faint, erythematous, macular skin rash over the trunk and abdomen. Laboratory studies reveal mild, normocytic, normochromic anemia and leukopenia with left shift. Peripheral blood smear is normal. Which of the following is the most likely route of transmission of this patient's infection?

A. Bite from a vector insect (40%)
B. Exposure to a carrier animal (6%)
✓ C. Ingestion of contaminated food (45%)
D. Inhalation of infectious droplets (4%)
E. Sexual contact with infected person (3%)

Correct

45%
Answered correctly

01 min, 16 secs
Time Spent

03/24/2021
Last Updated

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	Clinical manifestations of typhoid fever
Week 1	• Rising fever • Bacteremia • Relative bradycardia (pulse-temperature dissociation)
Week 2	• Abdominal pain • Rose spots on trunk & abdomen
Week 3	• Hepatosplenomegaly • Intestinal bleeding & perforation

Typhoid fever is a life-threatening infection caused by *Salmonella* Typhi or Paratyphi. These gram-negative, enteric pathogens reside only in the gastrointestinal tract of humans **(Choice B)**. Transmission occurs via the **fecal-oral route**, primarily due to ingestion of **food or water contaminated** by human feces. Therefore, most cases arise in the developing world where sanitation is poor. Travelers who have not been vaccinated (with typhoid vaccine) are at risk and may return clinically ill.

Typhoidal *Salmonella* species invade enterocytes, travel from the apical to the basolateral end of the cell in

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not been vaccinated (with typhoid vaccine) are at risk and may return clinically ill.

Typhoidal *Salmonella* species invade enterocytes, travel from the apical to the basolateral end of the cell in vacuoles, and emerge in the intestinal submucosa. Here, the organism is phagocytosed by macrophages but is able to evade destruction due to a specialized capsular antigen (Vi) that impairs the macrophage-mediated oxidative burst. The pathogen subsequently replicates in an unchecked fashion within macrophages and spreads through the lymphatic and reticuloendothelial system, leading to widespread, systemic illness.

Manifestations typically develop over weeks in a step-wise fashion. Patients usually develop a **progressive fever**, often with relative bradycardia (**pulse-temperature dissociation**), followed by abdominal pain, salmon-colored macules on the trunk (**"rose spots"**), and constipation or diarrhea. Dissemination through the reticuloendothelial system often causes hepatosplenomegaly, anemia, and leukopenia. Later, ulceration of Peyer patches (lymphoid aggregations in the small intestine submucosa) can result in gastrointestinal bleeding or intestinal perforation. Antibiotic treatment is required to prevent complications and death.

(Choice A) Malaria is transmitted by the bite of the female *Anopheles* mosquito and typically causes paroxysmal fever with nonspecific symptoms (eg, chills, fatigue, headache, myalgias). However, the fever

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(Choice A) Malaria is transmitted by the bite of the female *Anopheles* mosquito and typically causes paroxysmal fever with nonspecific symptoms (eg, chills, fatigue, headache, myalgias). However, the fever is almost always associated with tachycardia (not bradycardia), and peripheral blood smear will usually demonstrate the parasite and/or signs of red blood cell lysis.

(Choice D) Meningococcal meningitis is transmitted by aerosolized droplets from a carrier or infected patient and is associated with rapid-onset confusion, sepsis, hypotension, and a petechial/purpuric rash.

(Choice E) *Treponema pallidum*, the spirochete that causes syphilis, is transmitted sexually. Secondary syphilis is usually characterized by a widespread maculopapular rash that involves the palms and soles, generalized lymphadenopathy, and constitutional symptoms such as fever, headache, and myalgias. This patient's pulse-temperature dissociation, limited rash, and lack of adenopathy make syphilis less likely than typhoid fever.

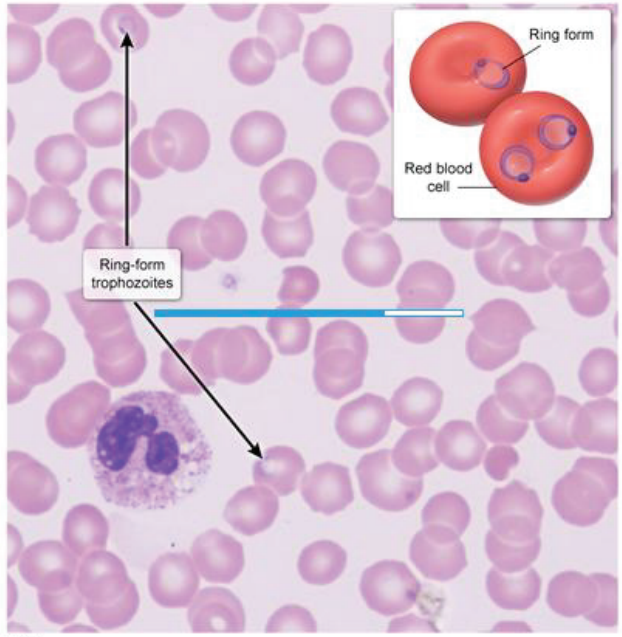
Educational objective:
Typhoid fever is caused by *Salmonella* Typhi or Paratyphi and presents with escalating fever, followed by abdominal pain, formation of rose spots on the chest/abdomen, and hemorrhagic enteritis with possible bowel perforation. Humans are the only reservoir; transmission is fecal-oral and primarily occurs due to ingestion of food or water contaminated with feces.

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Plasmodium



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ingestion of food or water contaminated with feces.

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A 4-year-old boy is brought to the office due to high fever, nasal discharge, and cough for 3 days. His family recently returned from a vacation in Mexico. Physical examination shows an ill-appearing, febrile child. The patient has bilateral conjunctival injection and several small white spots with an erythematous base on his buccal mucosa. A review of the medical record shows parental refusal of preventive health services in favor of a "natural" approach to the child's health. Over the next several days, which of the following is most likely to develop?

A. Jaundice
B. Maculopapular rash
C. Parotid swelling
D. Paroxysmal cough
E. Upper airway obstruction
F. Vesicular rash
G. Watery diarrhea

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family recently returned from a vacation in Mexico. Physical examination shows an ill-appearing, febrile child. The patient has bilateral conjunctival injection and several small white spots with an erythematous base on his buccal mucosa. A review of the medical record shows parental refusal of preventive health services in favor of a "natural" approach to the child's health. Over the next several days, which of the following is most likely to develop?

- A. ~~Jaundice~~ (1%)
- ✓ B. Maculopapular rash (77%)
- C. Parotid swelling (6%)
- D. Paroxysmal cough (4%)
- E. Upper airway obstruction (3%)
- F. Vesicular rash (4%)
- G. Watery diarrhea (1%)

Correct

77%
Answered correctly

01 min, 22 secs
Time Spent

12/28/2020
Last Updated

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Measles virus (rubeola)	
Clinical presentation	• Prodrome (eg, cough, coryza, conjunctivitis, fever, Koplik spots) • Maculopapular exanthem ○ Cephalocaudal & centrifugal spread ○ Spares palms/soles
Complications	• Primary measles pneumonia • Secondary bacterial infections (pneumonia & otitis media) • Neurologic ○ Encephalitis (within days) ○ Acute disseminated encephalomyelitis (within weeks) ○ Subacute sclerosing panencephalitis (within years)
Prevention	• Live attenuated measles vaccine

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Measles virus, or rubeola, is an enveloped, nonsegmented, negative-sense RNA virus of the Paramyxoviridae family. This highly contagious infection is **transmitted** by **airborne or person-to-person** contact. Classically, measles presents with a prodrome of **fever**, **cough**, **rhinorrhea**, and **conjunctivitis**. **Koplik spots** on the buccal mucosa are a pathognomonic finding and consist of small white, blue, or gray

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specks on an erythematous base. These symptoms precede a maculopapular exanthem that starts on the face and spreads down the trunk and extremities.

The parents' refusal of preventive medicine also supports a diagnosis of measles as the child likely did not receive the recommended combined measles, mumps, and rubella (MMR) vaccine. This live, attenuated vaccine is safe; serious side effects are extremely rare.

(Choice A) Hepatitis A spreads through the fecal-oral route and is generally an acute and self-limited disease. Hepatitis B is transmitted via bodily fluids and causes acute and chronic disease. These viruses cause elevated liver enzymes and hyperbilirubinemia (jaundice).

(Choice C) Mumps is a member of the Paramyxoviridae family and spreads by respiratory droplets or person-to-person contact. Infection classically causes parotitis, orchitis, and aseptic meningitis.

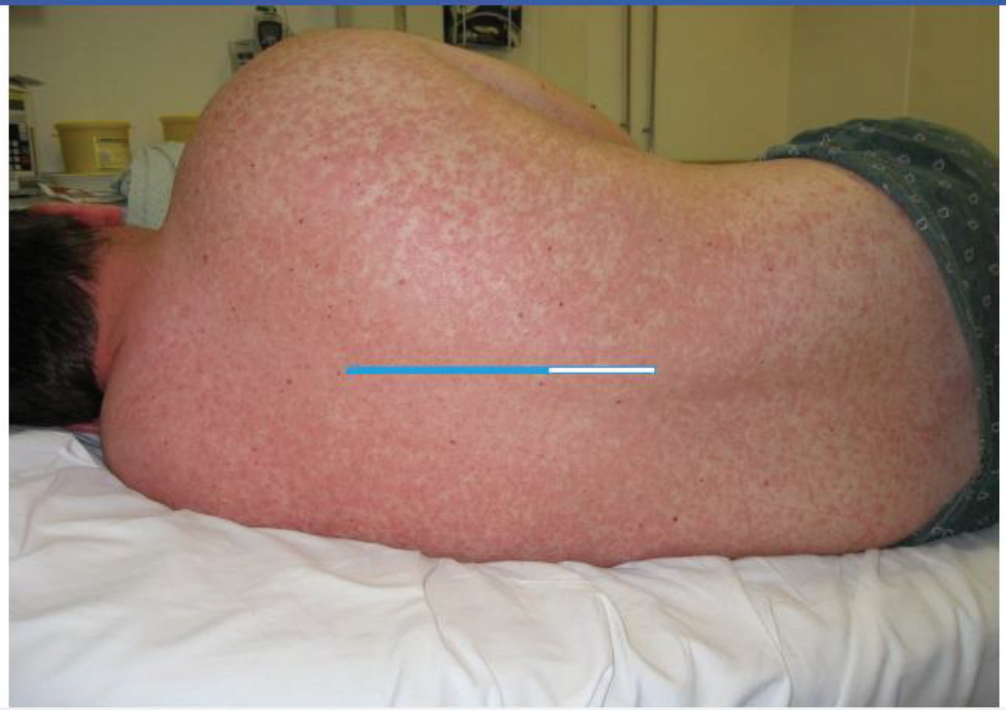
(Choice D) Pertussis is caused by the gram-negative bacteria *Bordetella pertussis* and spread by respiratory droplets. It is highly contagious and presents with paroxysms of cough and an inspiratory "whoop" sound in children.

(Choice E) Epiglottitis is linked with *Haemophilus influenzae* type b, a gram-negative, encapsulated bacteria spread by respiratory droplets. Patients often present with tripod positioning in an attempt to

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(Choice A) Hepati
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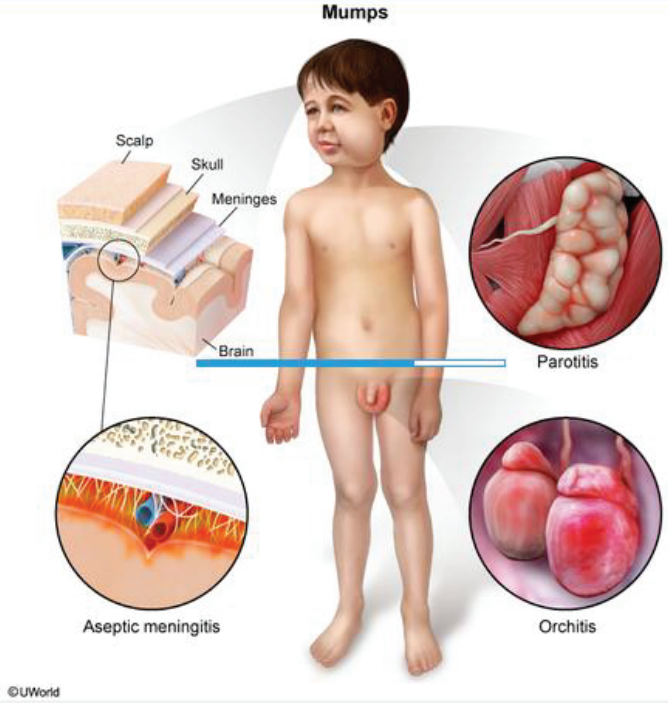
Standard pediatric immunizations in the United States	
Inactivated (killed)	• Polio • Hepatitis A • Influenza (injection)
Toxoid (inactivated toxin)	• Diphtheria, tetanus
Live attenuated	• Rotavirus • Measles • Mumps • Rubella • Varicella
Subunit/conjugate	• Hepatitis B • Pertussis • *Haemophilus influenzae* type B • Pneumococcal • Meningococcal • Human papillomavirus

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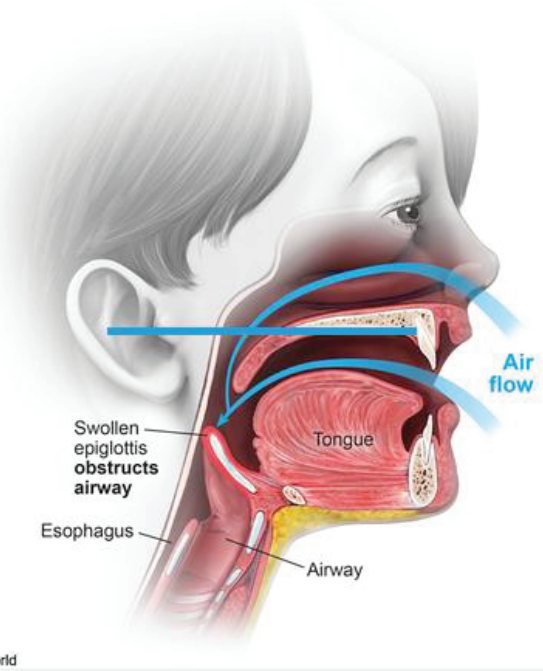
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Epiglottitis



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respiratory droplets. It is highly contagious and presents with paroxysms of cough and an inspiratory "whoop" sound in children.

(Choice E) Epiglottitis is linked with *Haemophilus influenzae* type b, a gram-negative, encapsulated bacteria spread by respiratory droplets. Patients often present with tripod positioning in an attempt to increase airflow due to life-threatening airway obstruction.

(Choice F) A diffuse vesicular rash of different stages is typical of chickenpox, or varicella-zoster virus (VZV) infection. VZV is a double-stranded, enveloped, DNA virus that is part of the Herpesviridae family. Transmission occurs via respiratory droplets or direct contact.

(Choice G) *Rotavirus*, a double-stranded RNA virus of the Reoviridae family, causes profuse watery diarrhea in infants, potentially leading to dehydration and death.

Educational objective:

Measles presents with fever, cough, rhinorrhea, and conjunctivitis followed by a maculopapular rash that starts on the face and spreads downwards. Koplik spots are pathognomonic for measles and characterized by tiny white or blue-gray lesions on the buccal mucosa.

References

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A 32-year-old woman comes to the office due to a small amount of malodorous vaginal discharge. She is sexually active with a male partner and uses condoms sporadically. The patient also requests testing for all sexually transmitted diseases because she is unsure if her partner is monogamous. She drinks a glass of wine every night with dinner and has had an abnormal Pap test in the past. Speculum examination reveals thin, gray discharge. Wet mount microscopy of the discharge shows large, atypical vaginal epithelial cells and no protozoa. Application of potassium hydroxide solution to the discharge yields a strong odor. Which of the following is the best treatment option for this patient?

A. Azithromycin
B. Ceftriaxone
C. Clindamycin
D. Fluconazole
E. Penicillin

Submit

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- A. Azithromycin (14%)
- B. Ceftriaxone (7%)
- ✓ C. Clindamycin (67%)
- D. Fluconazole (9%)
- E. Penicillin (1%)

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Differential diagnosis of vaginitis

Bacterial vaginosis (*Gardnerella vaginalis*)	Trichomoniasis (*Trichomonas vaginalis*)	Candida vaginitis (*Candida albicans*)
		
• Thin, off-white discharge with fishy odor • No inflammation	• Thin, yellow-green, malodorous, frothy discharge • Vaginal inflammation	• Thick, "cottage cheese" discharge • Vaginal inflammation
		
• pH >4.5 • Clue cells • Positive whiff test (amine odor with KOH)	• pH >4.5 • Motile trichomonads	• Normal pH (3.8 - 4.5) • Pseudohyphae
Metronidazole or clindamycin	Metronidazole; treat sexual partner	Fluconazole

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or clindamycin	partner	

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This patient has **bacterial vaginosis** (BV), an alteration in the normal vaginal flora associated with loss of lactobacilli and **overgrowth of anaerobes**, particularly the gram-variable rod ***Gardnerella vaginalis***. Although BV is not a sexually transmitted infection, it is associated with sexual activity (due to alterations of the vaginal flora from semen or contraceptives [eg, spermicide]).

Patients with BV commonly have a **thin, gray or clear** malodorous vaginal discharge. The discharge's odor becomes more prominent when **potassium hydroxide (KOH)** is added to a sample (**whiff test**) because of the volatilization of **amines** produced by *G vaginalis* and other anaerobes. **Clue cells** on wet mount microscopy are also characteristic.

Clindamycin and **metronidazole** are effective treatments for BV. Clindamycin is a bacteriostatic drug that inhibits protein translation by binding to the 50s ribosomal subunit. Metronidazole is bactericidal and damages the DNA of anaerobes; it is typically avoided with concurrent use of alcohol due to a disulfiram-like reaction (eg, vomiting, flushing).

(Choice A) *Chlamydia trachomatis* is an intracellular, gram-negative bacterium that can infect the columnar epithelium of the cervix (eg, cervicitis) and urethra, in addition to the lungs and eyes. Diagnosis is with nucleic acid amplification testing, and treatment is with azithromycin, a bacteriostatic macrolide

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(Choice A) *Chlamydia trachomatis* is an intracellular, gram-negative bacterium that can infect the columnar epithelium of the cervix (eg, cervicitis) and urethra, in addition to the lungs and eyes. Diagnosis is with nucleic acid amplification testing, and treatment is with azithromycin, a bacteriostatic macrolide antibiotic.

(Choice B) *Neisseria gonorrhoeae* is a gram-negative diplococcus that infects the genital mucosa (eg, cervicitis, urethritis) and is diagnosed with gram stain of discharge or nucleic acid amplification testing. It is treated with ceftriaxone (a third-generation cephalosporin that inhibits cell wall biosynthesis) monotherapy in the setting of negative testing for *Chlamydia*, and ceftriaxone plus doxycycline when *Chlamydia* coinfection is present.

(Choice D) Vulvovaginal candidiasis is typically due to *Candida albicans*, which causes vaginal pruritus, labial erythema, and a white, curd-like discharge. KOH examination shows yeast forms and pseudohyphae. Treatment is with azole antifungals (eg, fluconazole), which block ergosterol synthesis.

(Choice E) Syphilis causes a painless chancre (not vaginal discharge), followed by a rash and systemic symptoms; it is caused by the gram-negative spirochete *Treponema pallidum*. It is treated with penicillin, a bactericidal beta-lactam antibiotic that inhibits cell wall synthesis.

Educational objective:

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treated with ceftriaxone (a third-generation cephalosporin that inhibits cell wall biosynthesis) monotherapy in the setting of negative testing for *Chlamydia*, and ceftriaxone plus doxycycline when *Chlamydia* coinfection is present.

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Educational objective:
Bacterial vaginosis causes a thin, gray or clear, malodorous discharge from overgrowth of anaerobes (eg, *Gardnerella vaginalis*) and a loss of lactobacilli in the vaginal flora. Diagnosis is confirmed by the presence of clue cells and a positive amine whiff test with potassium hydroxide. Treatment is with clindamycin or metronidazole.

Pathology Infectious Diseases Bacterial vaginosis

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A 70-year-old man is diagnosed with a pulmonary nocardia infection. Medical conditions include hypertension and diet-controlled type 2 diabetes mellitus. Therapy is started with trimethoprim-sulfamethoxazole for a planned duration of 3-6 months. This patient is at greatest risk for which of the following drug-induced adverse effects?

- A. Esophagitis
- B. Hearing loss
- C. Hyperkalemia
- D. Pulmonary fibrosis
- E. Tendon rupture

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A 70-year-old man is diagnosed with a pulmonary nocardia infection. Medical conditions include hypertension and diet-controlled type 2 diabetes mellitus. Therapy is started with trimethoprim-sulfamethoxazole for a planned duration of 3-6 months. This patient is at greatest risk for which of the following drug-induced adverse effects?

- A. Esophagitis (11%)
- B. Hearing loss (8%)
- ✓ C. Hyperkalemia (67%)
- D. Pulmonary fibrosis (7%)
- E. Tendon rupture (4%)

Correct

67% Answered correctly

17 secs Time Spent

10/28/2020 Last Updated

Explanation

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Trimethoprim-sulfamethoxazole (TMP-SMX) is a combination of 2 bacteriostatic antibiotics that act synergistically to inhibit bacterial tetrahydrofolate formation, resulting in bactericidal activity. It has a broad spectrum of activity against many aerobic gram-positive and gram-negative bacteria and is commonly used for urinary tract infections, *Pneumocystis jiroveci* pneumonia, and *Nocardia* infections.

Common adverse effects of TMP-SMX include rash, nausea and vomiting, and folate deficiency (with prolonged use). In addition, **hyperkalemia** is a common adverse effect that can occur, regardless of dose. Similar to the actions of amiloride (a potassium-sparing diuretic), trimethoprim **blocks** the epithelial **sodium channel** in the distal tubule and collecting duct. This reduces transepithelial voltage and **impairs sodium-potassium exchange**, leading to reduced potassium excretion and hyperkalemia.

This effect is often magnified in the **elderly** population, those with renal failure, or those given other **potassium-sparing diuretics** (eg, spironolactone, amiloride), **ACE inhibitors** (eg, lisinopril), or angiotensin receptor blockers (eg, losartan). This patient with hypertension and diabetes may be receiving an ACE inhibitor, which further increases his risk of developing hyperkalemia.

(Choice A) Tetracyclines (eg, doxycycline, minocycline) and clindamycin are associated with esophagitis due to their low pH and irritant effects on the distal esophagus.

(Choice B) Aminoglycosides (eg, gentamycin, tobramycin) have broad-spectrum activity against aerobic

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(Choice A) Tetracyclines (eg, doxycycline, minocycline) and clindamycin are associated with esophagitis due to their low pH and irritant effects on the distal esophagus.

(Choice B) Aminoglycosides (eg, gentamycin, tobramycin) have broad-spectrum activity against aerobic gram-negative organisms and are most often used in severe gram-negative infections (eg, intraabdominal infections, osteomyelitis). These medications are associated with ototoxicity and may lead to tinnitus and hearing loss.

(Choice D) Nitrofurantoin has activity against many gram-positive and gram-negative urinary tract pathogens and is used for both acute treatment of urinary tract infections and long-term prophylaxis in patients with recurrent cystitis. It is associated with pneumonitis and pulmonary fibrosis.

(Choice E) Fluoroquinolones (eg, levofloxacin, ciprofloxacin) have activity against aerobic gram-negative rods and many respiratory pathogens. They are commonly used to treat pneumonia, pseudomonal infections, and urinary tract infections. These medications are associated with tendinopathy, including tendon rupture.

Educational objective:
Hyperkalemia is a common adverse effect of trimethoprim-sulfamethoxazole due to the trimethoprim-induced blockade of the sodium channels in the collecting duct, which prevents sodium-potassium exchange and reduces renal excretion of potassium (similar to the action of amiloride). This effect is often

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infections, osteomyelitis). These medications are associated with ototoxicity and may lead to tinnitus and hearing loss.

(Choice D) Nitrofurantoin has activity against many gram-positive and gram-negative urinary tract pathogens and is used for both acute treatment of urinary tract infections and long-term prophylaxis in patients with recurrent cystitis. It is associated with pneumonitis and pulmonary fibrosis.

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Educational objective:
Hyperkalemia is a common adverse effect of trimethoprim-sulfamethoxazole due to the trimethoprim-induced blockade of the sodium channels in the collecting duct, which prevents sodium-potassium exchange and reduces renal excretion of potassium (similar to the action of amiloride). This effect is often magnified in the elderly population, those with renal failure, or those given other potassium-sparing diuretics, ACE inhibitors, or angiotensin receptor blockers.

Pharmacology Infectious Diseases Hyperkalemia

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A 64-year-old man comes to the office for follow-up after a recent hospitalization. Ten days ago, he was admitted due to fever, dysuria, urinary urgency, and perineal pain. Evaluation revealed acute prostatitis, and urine culture was positive for *Escherichia coli* that was sensitive to all tested antibiotics. He received intravenous ciprofloxacin with improvement in his symptoms and was subsequently discharged on oral ciprofloxacin. The patient has been taking the antibiotic as prescribed, but over the past 2 days he has had recurrent fever and dysuria. He takes diltiazem for palpitations, atorvastatin for hyperlipidemia, and an over-the-counter antacid for frequent heartburn. Temperature is 37.3 C (99.1 F), blood pressure is 118/68 mm Hg, and pulse is 90/min. Physical examination shows a mildly enlarged and tender prostate. Repeat urine culture grows *E coli*. Which of the following is the most likely cause of this patient's recurrent symptoms?

A. Acquired antibiotic resistance
B. Decreased drug bioavailability
C. Exposure to untreated sexual partner
D. Increased renal drug clearance
E. Induction of hepatic CYP enzymes

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admitted due to fever, dysuria, urinary urgency, and perineal pain. Evaluation revealed acute prostatitis, and urine culture was positive for *Escherichia coli* that was sensitive to all tested antibiotics. He received intravenous ciprofloxacin with improvement in his symptoms and was subsequently discharged on oral ciprofloxacin. The patient has been taking the antibiotic as prescribed, but over the past 2 days he has had recurrent fever and dysuria. He takes diltiazem for palpitations, atorvastatin for hyperlipidemia, and an over-the-counter antacid for frequent heartburn. Temperature is 37.3 C (99.1 F), blood pressure is 118/68 mm Hg, and pulse is 90/min. Physical examination shows a mildly enlarged and tender prostate. Repeat urine culture grows *E coli*. Which of the following is the most likely cause of this patient's recurrent symptoms?

A. Acquired antibiotic resistance
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C. Exposure to untreated sexual partner
D. Increased renal drug clearance
E. Induction of hepatic CYP enzymes

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intravenous ciprofloxacin with improvement in his symptoms and was subsequently discharged on oral ciprofloxacin. The patient has been taking the antibiotic as prescribed, but over the past 2 days he has had recurrent fever and dysuria. He takes diltiazem for palpitations, atorvastatin for hyperlipidemia, and an over-the-counter antacid for frequent heartburn. Temperature is 37.3 C (99.1 F), blood pressure is 118/68 mm Hg, and pulse is 90/min. Physical examination shows a mildly enlarged and tender prostate. Repeat urine culture grows *E coli*. Which of the following is the most likely cause of this patient's recurrent symptoms?

A. Acquired antibiotic resistance (10%)
✓ B. Decreased drug bioavailability (57%)
C. Exposure to untreated sexual partner (2%)
D. Increased renal drug clearance (3%)
E. Induction of hepatic CYP enzymes (25%)

Correct
57%
01 min, 25 secs
01/30/2021

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Chelation drug interactions	
Mechanism	• Formation of insoluble compounds with polyvalent cations in the gastrointestinal tract • Decreased absorption of drug
Commonly involved drugs	• Tetracyclines • Fluoroquinolones • Levothyroxine
Chelation cations	• Iron • Calcium • Magnesium • Aluminum

This patient has had a relapse of acute prostatitis despite an adequate initial response and good medication adherence. This treatment failure is likely due to a **drug-drug interaction** with his home medications.

Fluoroquinolones normally have very high bioavailability and near complete absorption. However, they

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medication adherence. This treatment failure is likely due to a **drug-drug interaction** with his home medications.

Fluoroquinolones normally have very high bioavailability and near-complete absorption. However, they can form insoluble chelate complexes with **polyvalent cations** (eg, **calcium**, iron, aluminum, magnesium) in the gastrointestinal tract. This leads to **impaired absorption** and a significant decrease in drug bioavailability. In this patient's case, his initial response to the antibiotic reflects the parenteral dosing, which bypasses the gastrointestinal tract and avoids this potential interaction.

Over-the-counter **antacids** typically contain calcium, magnesium, and/or aluminum salts and are used by many patients for treatment of heartburn due to gastroesophageal reflux. Calcium salts (eg, calcium carbonate, calcium citrate) are also widely used in the treatment of osteoporosis. However, since these medications are available without a prescription and are often taken intermittently, the potential for interaction may not be apparent at the time antibiotic treatment is initiated.

(Choice A) Antimicrobial sensitivity testing of this patient's initial culture showed no significant fluoroquinolone resistance. In addition, he had a positive initial clinical response. Loss of effectiveness after changing to an oral formulation is more consistent with decreased bioavailability rather than antibiotic resistance.

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resistance.

(Choice C) Prostatitis due to sexually transmitted organisms is typically seen with *Neisseria gonorrhoeae* and *Chlamydia trachomatis* and is more common with younger rather than older men. Reinfection with *E coli* via sexual contact is unlikely.

(Choice D) Ciprofloxacin is primarily cleared by renal excretion, and the dosage may need to be decreased in patients with significant renal impairment. However, switching this patient from parenteral to oral antibiotic therapy would not affect renal drug clearance.

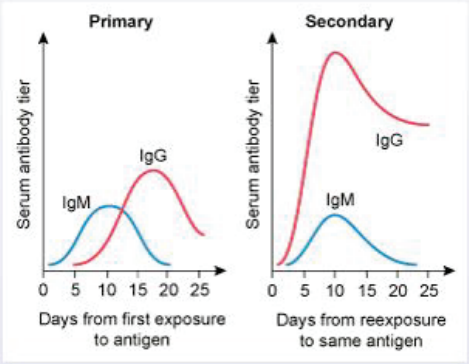
(Choice E) Diltiazem is a cytochrome P450 (CYP3A4) inhibitor (not inducer) that can cause increased systemic levels of numerous drugs, leading to drug toxicity (eg, myopathy due to statins). Regardless, ciprofloxacin is primarily eliminated by renal excretion, and drug levels are unlikely to be significantly affected by P450 inducers.

Educational objective:
Fluoroquinolones can form insoluble chelate complexes with polyvalent cations (eg, calcium, iron, aluminum, magnesium) in the gastrointestinal tract, leading to impaired absorption. This effect can be seen with over-the-counter antacids containing calcium, magnesium, and/or aluminum salts and in patients taking calcium salts (eg, calcium carbonate, calcium citrate) for treatment of osteoporosis.

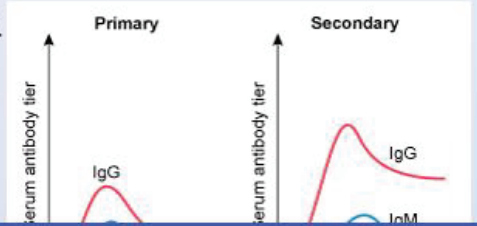
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A 4-year-old girl is brought to the clinic for her routine yearly visit. She has no chronic medical conditions and has received all previously recommended vaccinations. The patient is due to receive several vaccinations today including a second measles vaccine. Which of the following IgM and IgG trends is expected to occur after initial and subsequent measles vaccinations?

A.

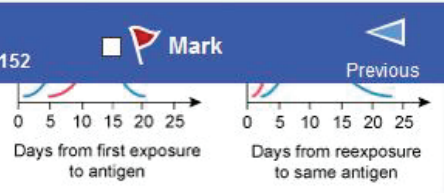


B.

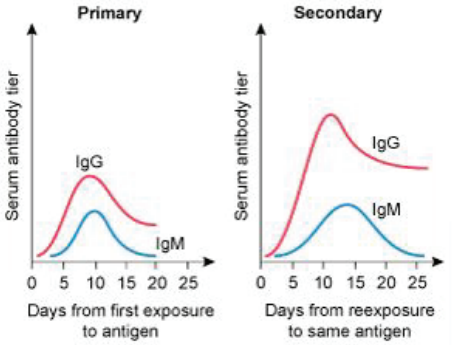


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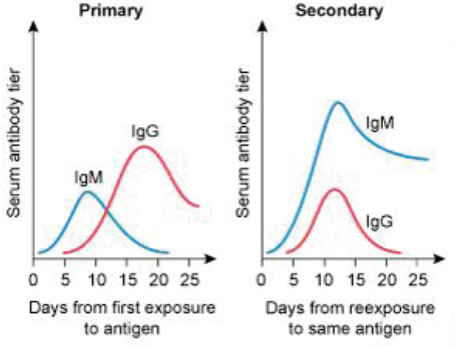
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B.



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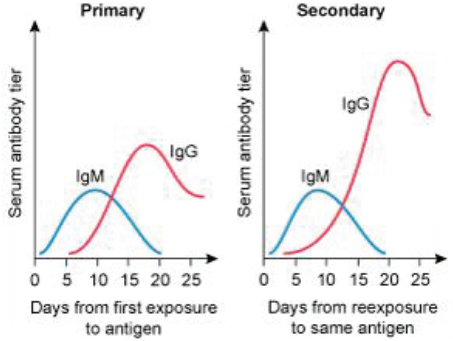


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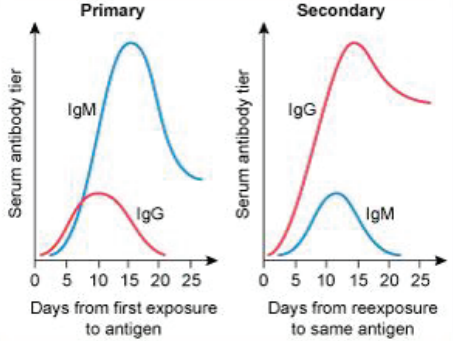
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to antigen to same antigen

D.



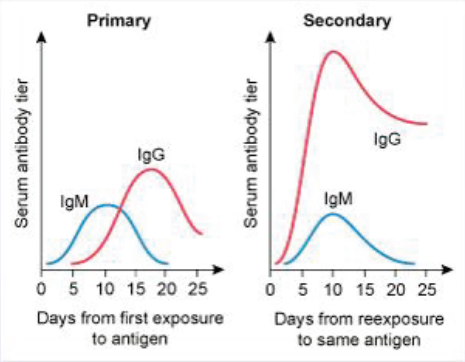
E.



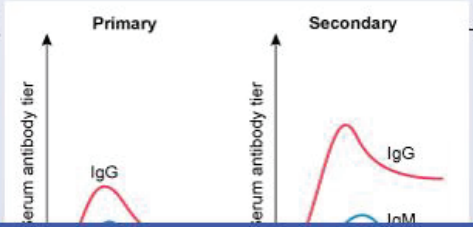
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A 4-year-old girl is brought to the clinic for her routine yearly visit. She has no chronic medical conditions and has received all previously recommended vaccinations. The patient is due to receive several vaccinations today including a second measles vaccine. Which of the following IgM and IgG trends is expected to occur after initial and subsequent measles vaccinations?

A. (60%)

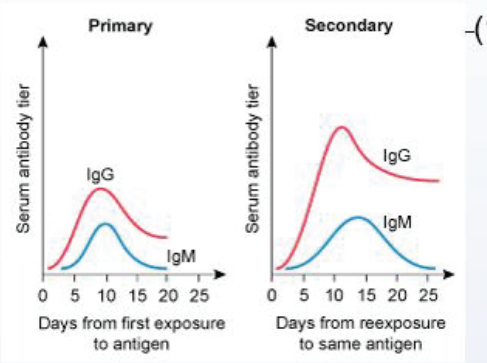


B. (1%)

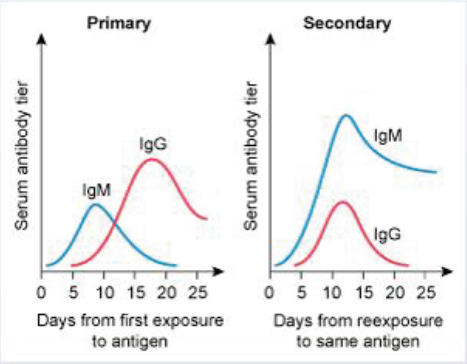


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B. (1%)



C. (1%)



D. (21%)

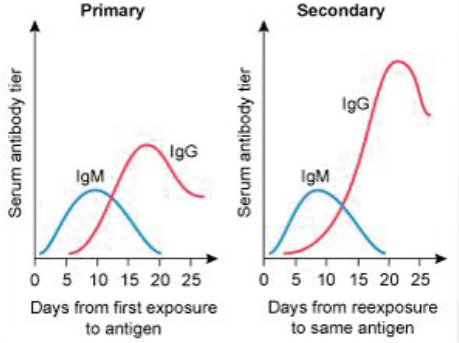


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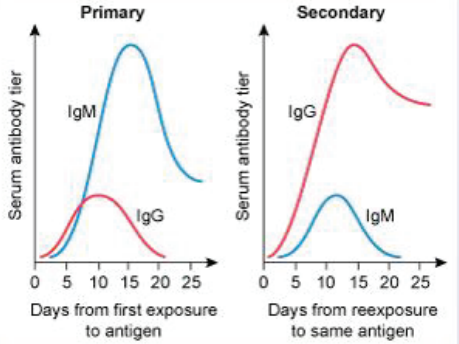
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to antigen to same antigen

D. (21%)

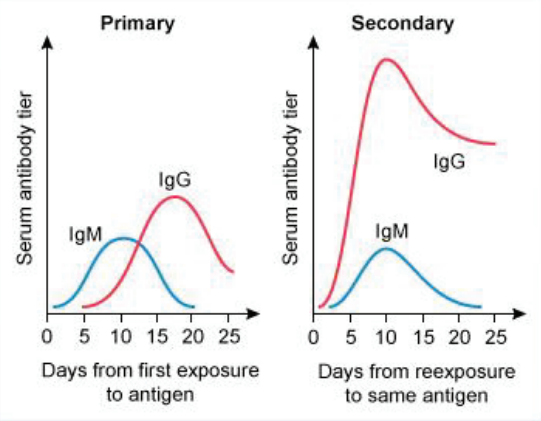


E. (14%)



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Explanation



Although B cells are the primary players in inducing a **vaccine response**, T cells play a key role in enabling high-affinity antibodies and immunological memory. Most vaccinations use peptide antigens or nonpeptides bonded to peptides (ie, conjugate vaccine) so the antigen can be displayed on MHC class II molecules on antigen-presenting cells (APCs), which leads to a much stronger T-cell–mediated immune response.

Vaccines given in series (eg, measles, mumps, and rubella) typically trigger the following immunologic

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response.

Vaccines given in series (eg, measles, mumps, and rubella) typically trigger the following immunologic changes:

- **Primary response**: Upon initial vaccination, foreign antigen binds to and activates B lymphocytes with compatible antigen receptors, leading to clonal B-cell expansion and differentiation into **short-lived plasma cells** that secrete low-affinity IgM. **Early production of IgM** can be detected in the serum within a few days of immunization. APCs also ingest the peptide and travel to regional lymph nodes where they stimulate CD4 T lymphocytes to interact with activated B cells. This interaction facilitates **immunoglobulin class switching** from IgM to other types (eg, IgG, IgA) and stimulates B-cell differentiation into memory B cells. Plasma cells secrete **high-affinity IgG**, and levels peak a few weeks after immunization (**after IgM peaks**) before slowly waning **(Choices B and E)**.
- **Secondary response:** subsequent vaccination or pathogen exposure results in a **IgM response similar to initial vaccination** due to stimulation of antigen-specific naïve B lymphocytes. However, the previously formed **memory B cells** quickly differentiate into long-lasting plasma cells to produce a **rapid and sustained IgG** response that peaks around the same time as the IgM response but is greater in magnitude **(Choices C and D)**. IgG rapidly neutralizes invading organisms and is

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- **Secondary response:** subsequent vaccination or pathogen exposure results in a **IgM response similar to initial vaccination** due to stimulation of antigen-specific naïve B lymphocytes. However, the previously formed **memory B cells** quickly differentiate into long-lasting plasma cells to produce a **rapid and sustained IgG** response that peaks around the same time as the IgM response but is greater in magnitude **(Choices C and D)**. IgG rapidly neutralizes invading organisms and is responsible for the protective effects of the vaccine.

Educational objective:

Initial vaccination generates an early IgM response by short-lived plasma cells followed by a delayed-onset, longer-lasting IgG response due to T-cell dependent class switching (IgM peaks before IgG). Due to formation of memory B cells, secondary responses (eg, booster vaccination, pathogen exposure) are characterized by a rapid and sustained IgG response with a short-term, more muted IgM response.

References

- How advances in immunology provide insight into improving vaccine efficacy.

Immunology	Infectious Diseases	Immunizations
Subject	System	Topic

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A 52-year-old man is evaluated for low-grade fever, malaise, abdominal pain, and diarrhea. The patient underwent a cadaveric renal transplant 6 months ago to treat renal failure from underlying polycystic kidney disease. He takes maintenance immunosuppressive therapy. Physical examination shows mild tenderness in the lower abdominal quadrants with no rebound tenderness. Serum immunosuppressant levels are within therapeutic range, and renal function studies are normal. Colonoscopy reveals mucosal erythema and ulcerations. Biopsy shows large cells with inclusion bodies, and a polymerase chain reaction-based test detects viral DNA. First-line therapy for the infection is initiated. This patient is at greatest risk of which of the following from the treatment?

A. Hepatitis
B. Myopathy
C. Neutropenia
D. Pancreatitis
E. Thyroiditis

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underwent a cadaveric renal transplant 6 months ago to treat renal failure from underlying polycystic kidney disease. He takes maintenance immunosuppressive therapy. Physical examination shows mild tenderness in the lower abdominal quadrants with no rebound tenderness. Serum immunosuppressant levels are within therapeutic range, and renal function studies are normal. Colonoscopy reveals mucosal erythema and ulcerations. Biopsy shows large cells with inclusion bodies, and a polymerase chain reaction-based test detects viral DNA. First-line therapy for the infection is initiated. This patient is at greatest risk of which of the following from the treatment?

- A. Hepatitis (23%)
- B. Myopathy (8%)
- C. Neutropenia (61%)
- D. ~~Pancreatitis~~ (5%)
- E. ~~Thyroiditis~~ (0%)

Incorrect
Correct answer

61%
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Patients who undergo organ transplantation and are on immunosuppressive therapy are at risk for **cytomegalovirus** (CMV) **reactivation** with end-organ disease (eg, colitis, retinitis, pneumonitis). This patient has classic manifestations of **CMV colitis** including fever, fatigue, abdominal pain, and diarrhea. Because serum testing for CMV DNA may be negative, patients with suspected CMV colitis usually undergo colonoscopy with biopsy. Typical findings include colonic mucosal erythema/ulcerations. Biopsy generally reveals **large cells** with intranuclear and intracytoplasmic inclusions ("owl's-eye" appearance).

First-line therapy for CMV colitis is intravenous **ganciclovir**. This guanine nucleoside analogue **interferes with viral DNA replication** by competitively inhibiting the incorporation of guanosine triphosphate into CMV DNA strands by CMV DNA polymerase. However, this drug also impedes human DNA polymerase to a lesser degree and can interfere with host cell replication, particularly in areas of high turnover (eg, hematologic progenitor cells). Therefore, ganciclovir is often associated with prominent hematologic side effects such as **neutropenia**, anemia, and thrombocytopenia.

(Choice A) The tuberculosis medications isoniazid and pyrazinamide can cause significant hepatotoxicity.

(Choice B) Myopathy and rhabdomyolysis can be associated with the use of integrase inhibitors (eg, raltegravir, dolutegravir) in the treatment of HIV.

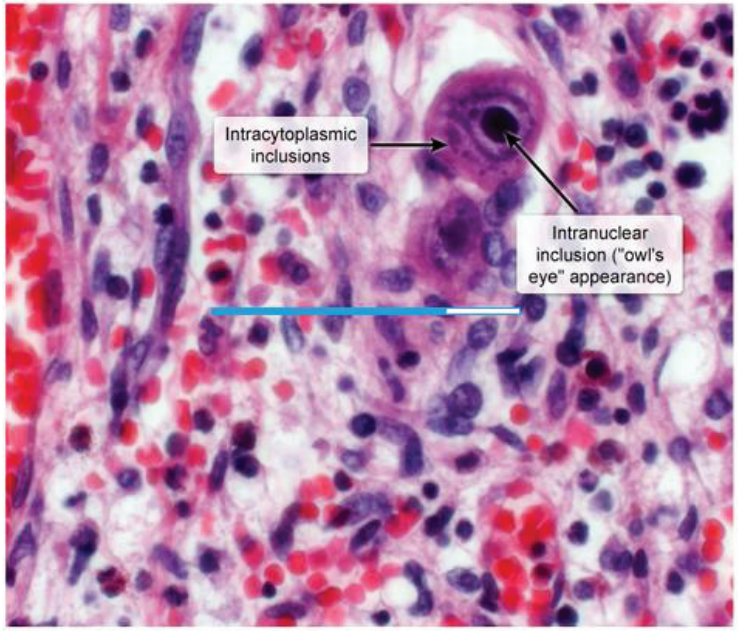
(Choice D) Pancreatitis is an important side effect of the HIV medication didanosine, a nucleoside reverse

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Cytomegalovirus



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(Choice D) Pancreatitis is an important side effect of the HIV medication didanosine, a nucleoside reverse

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hematologic progenitor cells). Therefore, ganciclovir is often associated with prominent hematologic side effects such as **neutropenia**, anemia, and thrombocytopenia.

(Choice A) The tuberculosis medications isoniazid and pyrazinamide can cause significant hepatotoxicity.

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(Choice D) Pancreatitis is an important side effect of the HIV medication didanosine, a nucleoside reverse transcriptase inhibitor.

(Choice E) Amiodarone is an antiarrhythmic medication that can cause hypothyroidism, hyperthyroidism, or thyroiditis.

Educational objective:
First-line therapy for CMV colitis and retinitis is ganciclovir. This medication inhibits viral synthesis by blocking CMV DNA polymerase. However, ganciclovir also blocks host DNA polymerase to a lesser degree, which can lead to hematologic side effects such as neutropenia, anemia, and thrombocytopenia.

Pharmacology | Infectious Diseases | Cytomegalovirus

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A phase II trial is being conducted at an academic medical center to assess the safety and efficacy of a novel antifungal medication that has yielded promising results in preclinical studies. The medication is known to inhibit fungal colony growth by changing the composition of the fungal cell membrane. Phase 0 and phase I trials on healthy volunteers have been uneventful. The current phase II trial includes 175 subjects. In 168 subjects, the new antifungal agent is found to inhibit liver cytochrome P450-dependent metabolism of several drugs. Based on these data, the new antifungal agent is most similar to which of the following?

A. Amphotericin B
B. Caspofungin
C. Flucytosine
D. Griseofulvin
E. Itraconazole

Submit

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A phase II trial is being conducted at an academic medical center to assess the safety and efficacy of a novel antifungal medication that has yielded promising results in preclinical studies. The medication is known to inhibit fungal colony growth by changing the composition of the fungal cell membrane. Phase 0 and phase I trials on healthy volunteers have been uneventful. The current phase II trial includes 175 subjects. In 168 subjects, the new antifungal agent is found to inhibit liver cytochrome P450-dependent metabolism of several drugs. Based on these data, the new antifungal agent is most similar to which of the following?

A. Amphotericin B (13%)
B. Caspofungin (5%)
C. Flucytosine (2%)
D. Griseofulvin (16%)
✓ E. Itraconazole (61%)

61% 22 secs 11/01/2020

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Azoles are antifungal medications that inhibit the demethylation of lanosterol into ergosterol in fungal cells. They exert their antifungal effects by suppressing synthesis of **ergosterol**, an essential component of the fungal cell **membrane**. However, azoles also **inhibit** the activity of the human **P450** cytochrome oxidase system. This property leads to multiple drug-drug **interactions**.

All azoles (eg, ketoconazole, fluconazole, itraconazole, voriconazole) increase the serum concentrations of drugs metabolized by liver P450 enzymes. This means that, when used concomitantly with azoles, drugs metabolized by the liver P450 system may have **increased** toxicity. For this reason, medications such as warfarin, cyclosporine, tacrolimus, and oral hypoglycemics should be avoided (or have their use carefully monitored) in patients who are receiving azole therapy.

Cytochrome oxidase inducers (eg, rifampin, phenytoin, carbamazepine, phenobarbital) increase azole metabolism, thereby lowering azole concentration in serum.

(Choice A) Amphotericin B is a polyene antifungal that binds ergosterol in the fungal cell membrane, leading to pore formation and cell lysis.

(Choice B) 1,3-beta-D-glucan is a major polysaccharide component of the fungal cell wall. Caspofungin and the other echinocandin antifungals block glucan synthesis.

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(Choice A) Amphotericin B is a polyene antifungal that binds ergosterol in the fungal cell membrane, leading to pore formation and cell lysis.

(Choice B) 1,3-beta-D-glucan is a major polysaccharide component of the fungal cell wall. Caspofungin and the other echinocandin antifungals block glucan synthesis.

(Choice C) Flucytosine inhibits the synthesis of both DNA (replication) and RNA (protein synthesis) in fungal cells. It is mainly used as a synergistic agent with amphotericin B. This drug combination is particularly important in the treatment of cryptococcal meningitis.

(Choice D) Griseofulvin, a P450 inducer, enters fungal cells and binds microtubules, inhibiting mitosis.

Educational objective:
Azoles inhibit the synthesis of ergosterol by the fungal cytochrome P450 enzymes. They also suppress the human P450 system, resulting in many drug-drug interactions.

Pharmacology	Infectious Diseases	Azoles
Subject	System	Topic

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Gram-positive bacteria are injected under the skin of experimental animals. Three days later, the animals are treated with antibiotic therapy. Aspirates taken from the infection site are plated on nutrient-rich agar. The isolated bacteria assume a spherical configuration when placed in an isotonic solution and disintegrate rapidly when placed in a hypotonic solution. Which of the following antibiotics was most likely administered to the animals in this experiment?

A. Azithromycin
B. Cefuroxime
C. Chloramphenicol
D. Ciprofloxacin
E. Doxycycline

Submit

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Gram-positive bacteria are injected under the skin of experimental animals. Three days later, the animals are treated with antibiotic therapy. Aspirates taken from the infection site are plated on nutrient-rich agar. The isolated bacteria assume a spherical configuration when placed in an isotonic solution and disintegrate rapidly when placed in a hypotonic solution. Which of the following antibiotics was most likely administered to the animals in this experiment?

- A. Azithromycin (9%)
- ✓ B. Cefuroxime (60%)
- C. Chloramphenicol (11%)
- D. Ciprofloxacin (8%)
- E. Doxycycline (9%)

Correct

60% Answered correctly

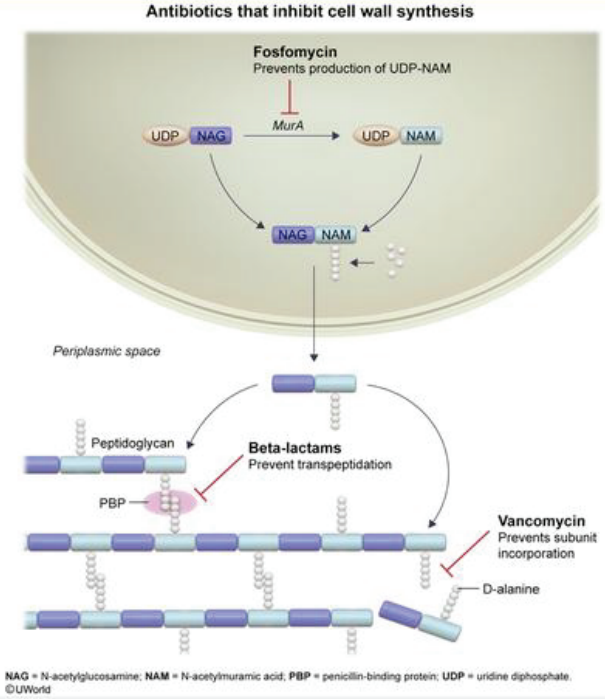
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NAG = N-acetylglucosamine; **NAM** = N-acetylmuramic acid; **PBP** = penicillin-binding protein; **UDP** = uridine diphosphate.
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The **bacterial cell wall** is composed of **rigid**, cross-linked peptidoglycan pentads on a glucosamine backbone. Its primary purpose is to provide **external structure** to the bacterium and **prevent disfigurement** or lysis in changing osmotic gradients. In this experiment, the assumption of a spherical shape in an isotonic solution and lysis in a hypotonic solution indicate **disruption** of the bacterial cell wall. Several classes of antibiotics target cell wall synthesis, including fosfomycin, vancomycin, penicillins, and **cephalosporins** (eg, **cefuroxime**).

(Choices A and C) Azithromycin and chloramphenicol inhibit the bacterial 50S ribosomal subunit. They have no effect on the cell wall and would not alter bacterial shape in different osmotic gradients. Side effects of chloramphenicol include dose-related myelosuppression and aplastic anemia.

(Choice D) Fluoroquinolones (eg, ciprofloxacin) inhibit bacterial DNA topoisomerase and gyrase, which results in bacterial cell death due to DNA damage. They do not affect the cell wall.

(Choice E) Doxycycline disrupts bacterial protein synthesis by inhibiting the bacterial 30S ribosomal subunit. It has no effect on the rigidity of the cell wall.

Educational objective:

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cephalosporins (eg, ceftriaxone).

(Choices A and C) Azithromycin and chloramphenicol inhibit the bacterial 50S ribosomal subunit. They have no effect on the cell wall and would not alter bacterial shape in different osmotic gradients. Side effects of chloramphenicol include dose-related myelosuppression and aplastic anemia.

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(Choice E) Doxycycline disrupts bacterial protein synthesis by inhibiting the bacterial 30S ribosomal subunit. It has no effect on the rigidity of the cell wall.

Educational objective:
The bacterial cell wall protects the organism from osmotic stress. Antibiotics that target the cell wall result in bacterial lysis in hypotonic solutions. Fosfomycin, vancomycin, penicillins, and cephalosporins all disrupt bacterial cell wall synthesis.

Pharmacology	Infectious Diseases	Cephalosporins
Subject	System	Topic

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A 25-year-old man comes to the office for follow-up. He was diagnosed with HIV several weeks ago following a hospitalization for *Pneumocystis* pneumonia. He has no other medical problems. His HIV drug susceptibility report shows no evidence of resistance. The patient's treatment regimen includes a drug that is structurally unrelated to nucleosides and is not phosphorylated intracellularly. The drug acts within the cytoplasm of infected cells to inhibit the synthesis of viral DNA from the RNA template. Which of the following agents was most likely used in this patient?

A. Emtricitabine
B. Enfuvirtide
C. Nevirapine
D. Ritonavir
E. Zidovudine

Submit

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A 25-year-old man comes to the office for follow-up. He was diagnosed with HIV several weeks ago following a hospitalization for *Pneumocystis* pneumonia. He has no other medical problems. His HIV drug susceptibility report shows no evidence of resistance. The patient's treatment regimen includes a drug that is structurally unrelated to nucleosides and is not phosphorylated intracellularly. The drug acts within the cytoplasm of infected cells to inhibit the synthesis of viral DNA from the RNA template. Which of the following agents was most likely used in this patient?

- A. Emtricitabine (8%)
- B. ~~Enfuvirtide~~ (12%)
- ✓ C. Nevirapine (37%)
- D. ~~Ritonavir~~ (20%)
- E. Zidovudine (20%)

Correct

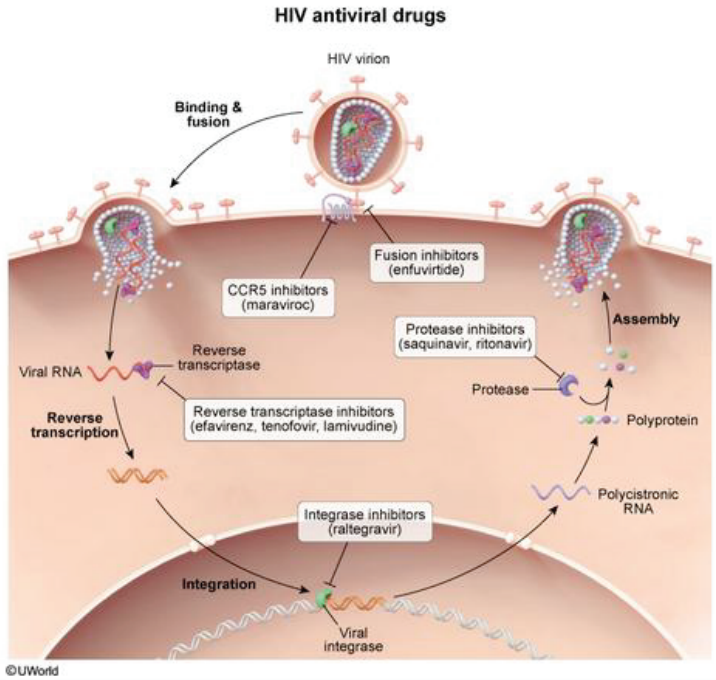
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Retroviral reverse transcriptase inhibitors prevent the synthesis of viral DNA from the RNA template. **Nonnucleoside reverse transcriptase inhibitors** (NNRTIs) do **not** require activation via intracellular phosphorylation. The more common NNRTIs include **nevirapine** and **efavirenz**. They are best used in conjunction with other antiretroviral agents for the treatment of HIV infection.

Adverse effects are common with NNRTIs. Abrupt-onset flulike symptoms, abdominal pain, jaundice, or fever may indicate potentially life-threatening **hepatic failure** (most likely to occur within the first 6 weeks of NNRTI therapy). Life-threatening skin reactions (eg, Stevens-Johnson syndrome, toxic epidermal necrolysis) have also been observed.

(Choices A and E) Zidovudine and emtricitabine are nucleoside reverse transcriptase inhibitors (NRTIs). In general, NRTIs must be converted into their monophosphate forms by a cellular kinase (cellular thymidine kinase) before they can be converted into pharmacologically active triphosphate forms.

(Choice B) Enfuvirtide is an HIV fusion inhibitor that binds to HIV envelope gp41 and blocks the conformational changes necessary for the fusion of viral and cellular membranes. Through this mechanism, enfuvirtide denies the HIV genome entry into uninfected $CD4^+$ T-cells. Its main site of action is outside the cytoplasm.

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Mechanism of action of HIV antiretroviral medications

Class	Example(s)	Mechanism of action
NRTI	Tenofovir, emtricitabine, lamivudine, abacavir, zidovudine	Inhibits HIV DNA synthesis from RNA template by terminating DNA chain elongation • NRTI: **Competitive** nucleoside/nucleotide RT inhibitor • NNRTI: **Allosteric** RT inhibitor
NNRTI	Efa**vir**enz, ne**vir**apine	
PI	Ataza**navir**, daru**navir**, indi**navir**, rito**navir**	Inhibits HIV polyprotein **cleavage**
Inte**gra**se inhibitor	Dolute**gravir**, ralte**gravir**	Inhibits HIV DNA integration into host genome
Fusion inhibitor	En**fu**virtide	Inhibits HIV fusion with target cell membrane by binding to HIV **gp41**
CCR5 antagonist	Maraviroc	Inhibits HIV entry by blocking the HIV **gp120 allosteric** interaction with CCR5 (tropism testing required)

CCR5 = chemokine (C-C motif) receptor 5; **NNRTI** = non-nucleoside reverse transcriptase inhibitor; **NRTI** = nucleoside/nucleotide reverse transcriptase inhibitor; **PI** = protease inhibitor; **RT** = reverse transcriptase.

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(Choices A and E) Zidovudine and emtricitabine are nucleoside reverse transcriptase inhibitors (NRTIs). In general, NRTIs must be converted into their monophosphate forms by a cellular kinase (cellular thymidine kinase) before they can be converted into pharmacologically active triphosphate forms.

(Choice B) Enfuvirtide is an HIV fusion inhibitor that binds to HIV envelope gp41 and blocks the conformational changes necessary for the fusion of viral and cellular membranes. Through this mechanism, enfuvirtide denies the HIV genome entry into uninfected $CD4^+$ T-cells. Its main site of action is outside the cytoplasm.

(Choice D) Ritonavir is an inhibitor of HIV protease that prevents assembly and maturation of the virus. Nonfunctional, noninfectious virions are produced instead. Reverse transcription is not affected.

Educational objective:
Nonnucleoside reverse transcriptase inhibitors (NNRTIs) are antiretroviral drugs that do not require activation via intracellular phosphorylation. The more common NNRTIs include nevirapine and efavirenz.

Pharmacology	Infectious Diseases	Antiretroviral therapy
Subject	System	Topic

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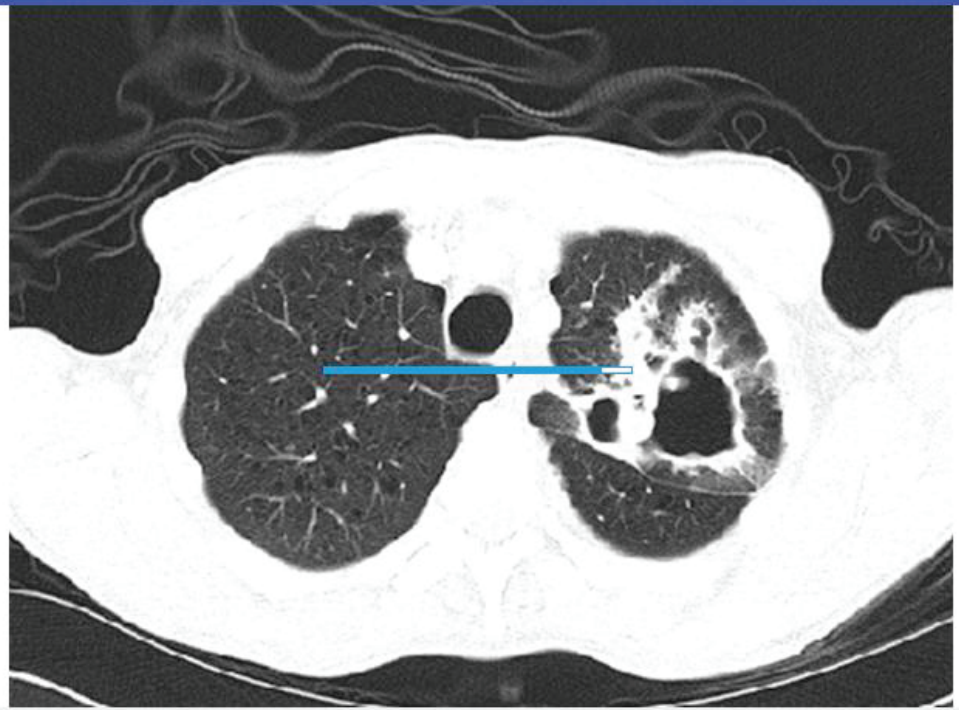
A 57-year-old man comes to the office due to 2 months of progressive cough and weight loss. He has a history of diabetes mellitus type 2 and chronic kidney disease. He does not smoke cigarettes. The patient traveled to Denmark 4 months ago for a 2-week vacation. He has 2 cats and a bird. He works in the maintenance department of a large hotel and services the hot tub and swimming pools. Temperature is 38 C (100.4 F), blood pressure is 140/100 mm Hg, pulse is 88/min, and respirations are 16/min. The patient is 190 cm (6 foot 3 inches) tall. BMI is 22 kg/m^2. Examination shows cervical lymphadenopathy. Chest imaging is shown in the exhibit. Hemoglobin A1c is 8.5% and serum creatinine is 3.8 mg/dL. Which of the following risk factors most likely contributed to this patient's current condition?

A. Body habitus
B. Hot tub cleaning
C. Living with pets
D. Travel to Denmark
E. Underlying medical conditions

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history of diabetes mellitus type 2 and chronic kidney disease. He does not smoke cigarettes. The patient traveled to Denmark 4 months ago for a 2-week vacation. He has 2 cats and a bird. He works in the maintenance department of a large hotel and services the hot tub and swimming pools. Temperature is 38 C (100.4 F), blood pressure is 140/100 mm Hg, pulse is 88/min, and respirations are 16/min. The patient is 190 cm (6 foot 3 inches) tall. BMI is 22 kg/m^2. Examination shows cervical lymphadenopathy. Chest imaging is shown in the exhibit. Hemoglobin A1c is 8.5% and serum creatinine is 3.8 mg/dL. Which of the following risk factors most likely contributed to this patient's current condition?

A. ~~Body habitus~~ (2%)
B. Hot tub cleaning (23%)
C. Living with pets (26%)
D. ~~Travel to Denmark~~ (7%)
✓ E. Underlying medical conditions (39%)

Correct
39%
01 min, 38 secs
02/04/2021

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Host factors that increase the risk of active tuberculosis	
Immunosuppression	• HIV • Glucocorticoid use • TNF-α inhibitors
Chronic diseases	• Diabetes mellitus • Renal disease • Malignancy
Substance abuse	• Illicit drug use • Alcoholism • Tobacco use
Malnutrition	• Underweight (BMI <18.5 kg/m^2) • Vitamin D deficiency

TNF-α = tumor necrosis factor-alpha.

This patient's chronic cough, weight loss, cervical lymphadenopathy, and cavitary pulmonary lesion suggest

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TNF-α = tumor necrosis factor-alpha.

This patient's chronic cough, weight loss, cervical lymphadenopathy, and cavitary pulmonary lesion suggest **active pulmonary tuberculosis** (TB). Exposure to *Mycobacterium tuberculosis* usually results in lifelong latent infection due to the formation of granulomas, which wall off the pathogen and limit spread. However, the formation and maintenance of granulomas rely on coordination between monocytes and T lymphocytes. **Host conditions** that weaken these aspects of immune function often significantly increase the risk of reactivation TB; these include the following:

- **Chronic kidney disease** is associated with impaired function of monocytes and the cell-mediated immune response due to uremia and hypoalbuminemia. Risk of TB is increased 6- to 50-fold in this population and is greatest in those with end-stage disease.
- **Poorly controlled diabetes mellitus** is associated with immune impairment and alterations to cytokine signaling, which weaken the development and maintenance of granulomas. Risk of TB is greatest in those with chronic hyperglycemia (eg, this patient with hemoglobin A1c of 8.5%).

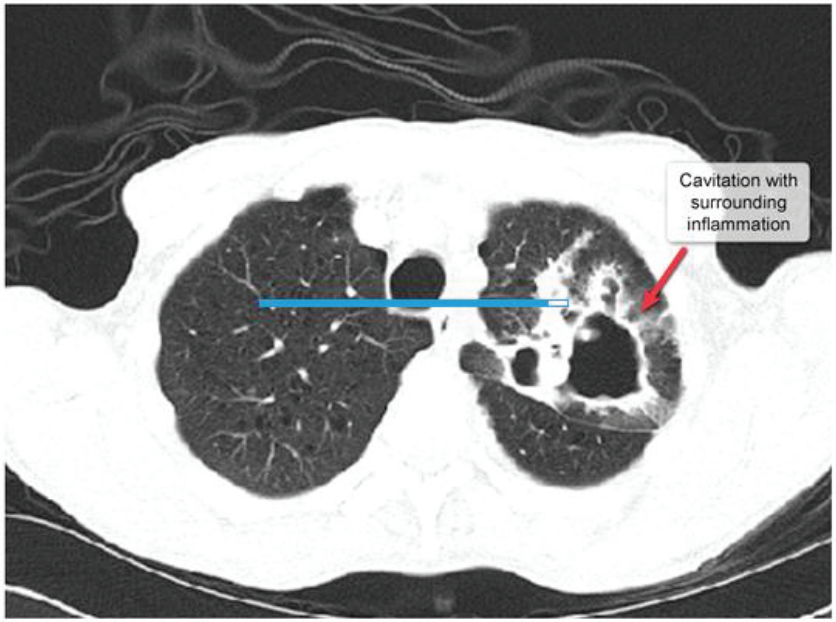
Increased risk of reactivation TB is also seen in those with immunosuppression (eg, HIV, immunomodulatory/glucocorticoid medications), substance abuse, malnutrition, and advanced age.

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Exhibit Display

Tuberculosis

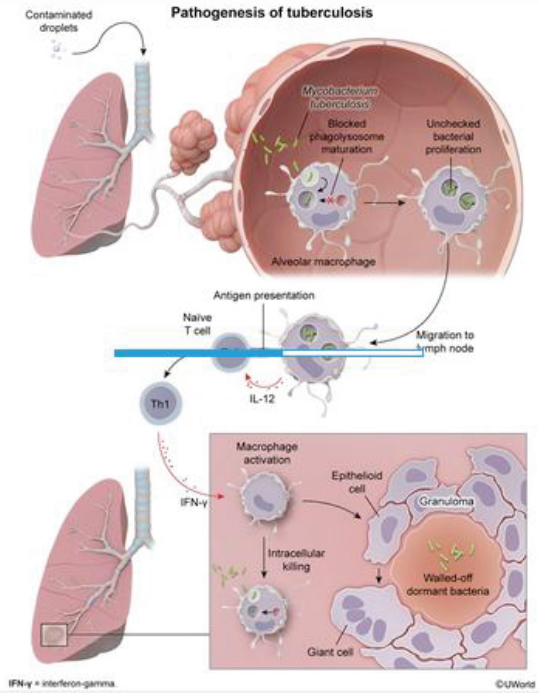


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(Choice A) A tall body habitus is often seen in Marfan syndrome. Although these individuals have an increased risk of spontaneous pneumothorax, manifestations would include acute shortness of breath and imaging evidence of air between the lung and chest wall.

(Choice B) Patients who work with hot tubs and swimming pools can develop hypersensitivity pneumonitis due to inhalation of *Mycobacterium avium*, a nontuberculous mycobacterium. Although most cases are marked by acute dyspnea, chronic symptoms can occur. However, imaging would generally show patchy, ground-glass pulmonary infiltrates, not a cavitary lesion.

(Choice C) Living with pets increases the risk of asthma due to increased exposure to allergens. Asthma is typically marked by recurrent bronchoconstriction with acute periods of dyspnea, wheeze, and cough. Chest x-ray may show hyperinflation and bronchial thickening but not cavitary infiltration.

(Choice D) Travel to areas endemic for TB can increase risk of exposure and subsequent infection. Endemic regions include India, sub-Saharan Africa, and Southeast Asia. Denmark has a low incidence of TB; it is unlikely that the patient acquired the infection during his visit to this country.

Educational objective:

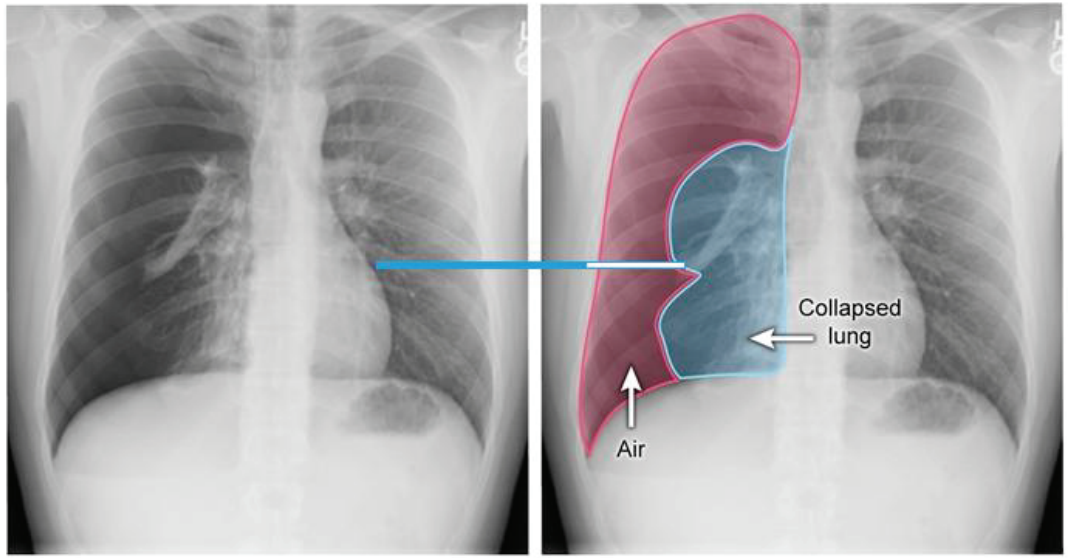
Mycobacterium tuberculosis infection is controlled by coordination between macrophages and T lymphocytes. Conditions that impair immune function increase the risk of active tuberculosis; this includes

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Exhibit Display

Pneumothorax



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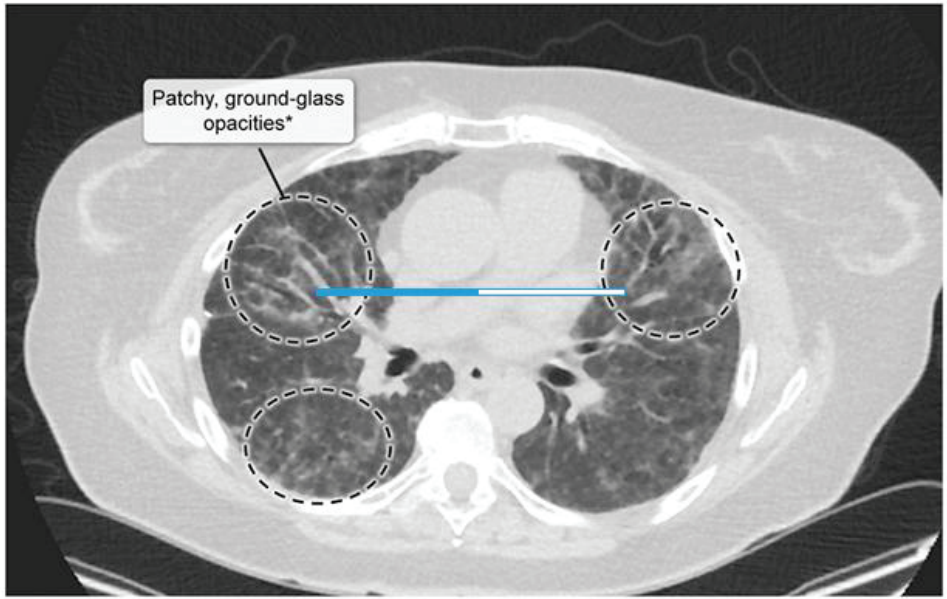
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Exhibit Display

Hypersensitivity pneumonitis



*Widespread inflammatory response causing diffuse alveolar damage with interstitial infiltrates

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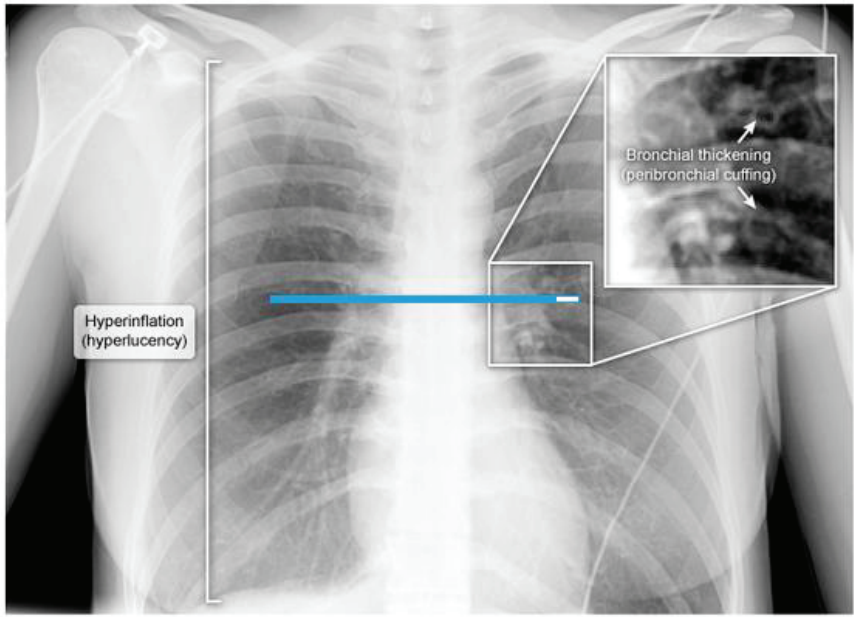
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Exhibit Display

Asthma exacerbation



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(Choice D) Travel to areas endemic for TB can increase risk of exposure and subsequent infection. Endemic regions include India, sub-Saharan Africa, and Southeast Asia. Denmark has a low incidence of TB; it is unlikely that the patient acquired the infection during his visit to this country.

Educational objective:
Mycobacterium tuberculosis infection is controlled by coordination between macrophages and T lymphocytes. Conditions that impair immune function increase the risk of active tuberculosis; this includes chronic kidney disease, diabetes mellitus, HIV, substance abuse, malnutrition, and advanced age.

Microbiology	Infectious Diseases	Tuberculosis
Subject	System	Topic

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A 29-year-old woman comes to the office due to severe joint pain in her hands, wrists, and ankles for a week. The pain is so severe that she is unable to perform her daily activities, and taking ibuprofen provides only partial relief. She has no prior medical conditions but developed high fever and diffuse rash during a trip to Puerto Rico 2 weeks ago. Evaluation at a local medical facility was negative for malaria, and her symptoms improved spontaneously after several days. She does not use tobacco, alcohol, or illicit drugs and is in a monogamous relationship with her husband. Temperature is 37 C (98.6 F), blood pressure is 122/70 mm Hg, and pulse is 86/min. Physical examination shows pink, moist oropharyngeal mucosa; no rash; clear lungs; normal heart sounds; and no abdominal organomegaly. There is periarticular swelling and tenderness of the wrists, ankles, and interphalangeal joints of her hands. Range of motion in these joints is decreased due to pain. Laboratory testing reveals lymphopenia. Which of the following is the most likely cause of this patient's joint pain?

A. Acute joint inflammation from crystal deposition
B. Immune-mediated inflammatory arthritis
C. Spondyloarthritis triggered by bacterial infection
D. Tick bite-borne spirochetal joint infection

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A. Acute joint inflammation from crystal deposition
B. Immune-mediated inflammatory arthritis
C. Spondyloarthritis triggered by bacterial infection
D. Tick bite-borne spirochetal joint infection
E. Viral infection transmitted by mosquito bite

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A. ~~Acute joint inflammation from crystal deposition~~ (0%)
B. Immune-mediated inflammatory arthritis (24%)
C. Spondyloarthritis triggered by bacterial infection (13%)
D. Tick bite-borne spirochetal joint infection (16%)
E. Viral infection transmitted by mosquito bite (45%)

45%
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02/05/2021

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Chikungunya fever	
Epidemiology	• Tropical/subtropical parts of Central/South America, Africa & Asia • Vector: *Aedes* **mosquito** (also transmits dengue & Zika)
Manifestations	• Incubation period: 3-7 days • High fevers & **severe polyarthralgias** (almost always present) • Headache, myalgias, conjunctivitis, maculopapular rash • Lymphopenia, thrombocytopenia, transaminitis
Management	• Supportive care (initial symptoms usually resolve in 7-10 days) • **Chronic arthralgias/arthritis** occurs in >50% (may require methotrexate)

This patient's transient febrile illness and rash followed by severe polyarthritis raise strong suspicion for **chikungunya**, an **alphavirus** transmitted to humans by *Aedes* **mosquitos** during blood feeding. Outbreaks are common in tropical and subtropical climates (eg, **Puerto Rico**, Africa, Asia, Indian/Pacific islands) during the rainy season and may be brought back to the United States by travelers.

Chikungunya means "stooped walk" because the hallmark of the disease is **severe joint symptoms**.

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islands) during the rainy season and may be brought back to the United States by travelers.

Chikungunya means "stooped walk" because the hallmark of the disease is **severe joint symptoms**. Manifestations generally begin a few days after transmission with high fever, symmetric **polyarticular arthralgia**, and a maculopapular rash. Lymphopenia and thrombocytopenia commonly occur. Initial symptoms usually abate completely within days, but >50% of individuals develop relapsed/chronic arthralgia, **polyarticular arthritis** (particularly of the wrists/hands/ankles), or tenosynovitis in the following weeks or months. Because *Aedes* mosquitos also transmit dengue and Zika viruses, coinfection can occur.

(Choice A) Gout causes recurrent, acute joint inflammation due to monosodium urate crystal deposition. However, most cases are monoarticular and occur in lower extremity joints.

(Choice B) Rheumatoid arthritis is an immune-mediated disorder that causes symmetric, inflammatory polyarthritis with eventual joint destruction. Patients generally develop morning stiffness followed by joint swelling in the fingers, wrists, and toes. Given this patient's young age, febrile illness with rash during recent travel, and lymphopenia, chikungunya is more likely.

(Choice C) Reactive arthritis is a rare condition that primarily occurs following a gastrointestinal (eg, *Salmonella*, *Shigella*, *Campylobacter*) or genital (eg, *Chlamydia*) bacterial infection. Manifestations

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recent travel, and lymphopenia, chikungunya is more likely.

(Choice C) Reactive arthritis is a rare condition that primarily occurs following a gastrointestinal (eg, *Salmonella*, *Shigella*, *Campylobacter*) or genital (eg, *Chlamydia*) bacterial infection. Manifestations typically include an asymmetric oligoarthritis that often affects the knees. This patient's symmetric polyarthritis following a febrile illness while traveling makes chikungunya far more likely.

(Choice D) Lyme disease is caused by the spirochete *Borrelia burgdorferi*. Initial symptoms can include fever, malaise, and a spreading, annular rash (erythema migrans). Several months or years later, late manifestations such as monoarticular arthritis of the knee or asymmetric oligoarthritis can also occur. This patient's polyarticular arthritis developing a few weeks after a febrile illness makes chikungunya far more likely.

Educational objective:

Chikungunya is an alphavirus spread by mosquitos to humans in tropical and subtropical areas. Initial manifestations include self-limited fever, severe polyarthralgia, and rash. Relapsed or chronic arthralgias, polyarthritis (eg, wrist, fingers, ankles), or tenosynovitis occur in >50% of infected individuals.

References

- Chikungunya infection: a re-emerging epidemic.

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A 74-year-old man is hospitalized with acute urinary retention complicated by urosepsis. He has a urinary catheter placed and is started on intravenous antibiotics. The patient requires endotracheal intubation and mechanical ventilation for 24 hours but is extubated successfully on the second hospitalization day. On the third day of hospitalization, he develops fever and right jaw pain. Physical examination shows firm swelling of the preauricular area on the right side extending to the angle of the mandible. Which of the following serum markers is most helpful for confirming the diagnosis?

- A. Alkaline phosphatase
- B. Amylase
- C. Gamma-glutamyl transpeptidase
- D. Lipase
- E. Parathyroid hormone

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A 74-year-old man is hospitalized with acute urinary retention complicated by urosepsis. He has a urinary catheter placed and is started on intravenous antibiotics. The patient requires endotracheal intubation and mechanical ventilation for 24 hours but is extubated successfully on the second hospitalization day. On the third day of hospitalization, he develops fever and right jaw pain. Physical examination shows firm swelling of the preauricular area on the right side extending to the angle of the mandible. Which of the following serum markers is most helpful for confirming the diagnosis?

A. Alkaline phosphatase (25%)
B. Amylase (50%)
C. Gamma-glutamyl transpeptidase (15%)
D. Lipase (4%)
E. Parathyroid hormone (4%)

Correct

50% Answered correctly

52 secs Time Spent

02/07/2021 Last Updated

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Suppurative parotitis in adults	
Risk factors	Decreased **salivary flow** • Medications (eg, **anticholinergics**) • Obstruction (eg, **calculi**, neoplasm) • **Dehydration**, postsurgical/**intubation**
Microbiology	• ***Staphylococcus aureus***, anaerobes
Clinical presentation	• Firm, erythematous pre/postauricular swelling • Trismus, dysphagia, systemic findings (fever, chills)
Diagnosis	• Imaging (ultrasound/CT): Ductal inflammation/obstruction, frank abscess • Laboratory: Elevated serum **amylase** without pancreatitis

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This patient's presentation suggests **parotitis**, an acute viral or bacterial infection of the parotid gland. Acute bacterial suppurative parotitis can be due to ***Staphylococcus aureus*** (most common) or mixed oral aerobes/anaerobes. Risk factors include **dehydration, intubation** (elderly postoperative patients), medications that decrease salivary flow (eg, **anticholinergics**), salivary flow obstruction (eg, salivary **calculi**, oral cavitary neoplasm), or recent intense tooth cleaning

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calculi, oral cavitary neoplasm), or recent intense teeth cleaning.

Suppurative parotitis usually presents with acute onset of firm and erythematous pre/postauricular **swelling** that extends to the mandible. Patients can also develop trismus, dysphagia, and systemic findings (eg, fever, chills). The diagnosis can be confirmed by **imaging** (eg, ultrasound, CT) showing parotid duct inflammation, obstruction by a stone, or sometimes abscess. As the parotid gland secretes **amylase**, suppurative parotitis can present with elevated serum amylase. However, affected patients have normal serum lipase levels without clinical evidence of pancreatitis **(Choice D)**.

(Choice A) Alkaline phosphatase is an enzyme that hydrolyzes and removes phosphate from other compounds (eg, proteins, enzymes). It is mainly found in the bone, liver, bile ducts, and placenta. Alkaline phosphatase can be elevated in biliary conditions, bone disease (eg, osteomalacia), and leukemia/lymphoma. However, it is usually not affected by parotitis.

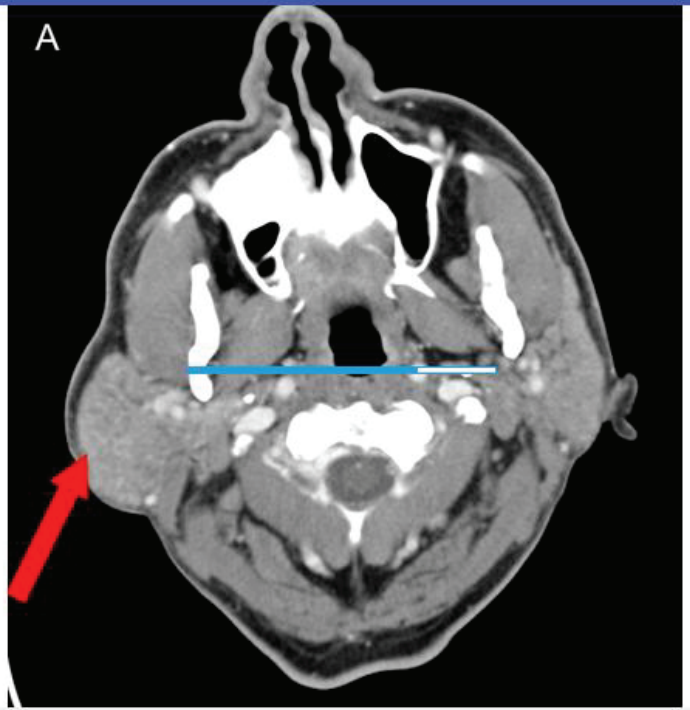
(Choice C) Gamma-glutamyl transpeptidase (GGT) helps convert glutathione to glutamate. It can be found in many organs, including the liver. GGT elevation suggests that alkaline phosphatase elevation is due to liver (not bone) pathology.

(Choice E) Parathyroid hormone (PTH) is secreted by the chief cells of the parathyroid gland and increases serum calcium to maintain calcium homeostasis. PTH has effects on the kidney and bone but is

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(Choice E) Parathyroid hormone (PTH) is secreted by the chief cells of the parathyroid gland and increases serum calcium to maintain calcium homeostasis. PTH has effects on the kidney and bone but is not elevated with parotitis.

Educational objective:

Acute bacterial parotitis occurs more commonly in elderly postoperative patients who are intubated or dehydrated. *Staphylococcus aureus* is the most common bacterial etiology. Diagnosis can be confirmed by imaging and an elevated serum amylase level (with a normal serum lipase level and no evidence of pancreatitis).

References

- Acute bacterial suppurative parotitis: microbiology and management.
- Acute postsurgical suppurative parotitis: current prevalence at Hospital das Clínicas, São Paulo University Medical School.

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A 48-year-old man comes to the hospital due to 10 days of persistent fever, chills, fatigue, and dyspnea. He had a splenectomy at age 28 after a motor vehicle accident and received the appropriate vaccines. The patient does not use tobacco, alcohol, or illicit drugs. He recently traveled from New York City to Connecticut for a family wedding. His temperature is 38.6 C (101.5 F), blood pressure is 118/70 mm Hg, and pulse is 108/min. Lung examination reveals coarse crackles. Laboratory studies are as follows:

Complete blood count	
Hemoglobin	9.6 g/dL
Reticulocytes	4%
Platelets	108,000/mm^3
Leukocytes	11,000/mm^3
Liver function studies	
Total bilirubin	1.8 mg/dL
Direct bilirubin	0.6 mg/dL

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Total bilirubin	1.8 mg/dL
Direct bilirubin	0.6 mg/dL
Alkaline phosphatase	120 U/L
Aspartate aminotransferase (SGOT)	87 U/L
Alanine aminotransferase (SGPT)	74 U/L
Lactate dehydrogenase	188 U/L (normal: 60-100 U/L)
Haptoglobin	36 mg/dL (normal: 50-150 mg/dL)

Chest x-ray reveals bilateral infiltrates. A peripheral blood smear shows normocytic, normochromic anemia with ring- and cross-shaped intraerythrocytic inclusions. The vector responsible for this patient's current condition can also transmit which of the following organisms?

A. *Borrelia burgdorferi*

B. Dengue virus

C. *Haemophilus influenzae*

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Lactate dehydrogenase	188 U/L (normal: 60-100 U/L)
Haptoglobin	36 mg/dL (normal: 50-150 mg/dL)

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A. *Borrelia burgdorferi*
B. Dengue virus
C. *Haemophilus influenzae*
D. *Histoplasma capsulatum*
E. *Neisseria meningitidis*
F. *Plasmodium falciparum*

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Lactate dehydrogenase	188 U/L (normal: 60-100 U/L)
Haptoglobin	36 mg/dL (normal: 50-150 mg/dL)

Chest x-ray reveals bilateral infiltrates. A peripheral blood smear shows normocytic, normochromic anemia with ring- and cross-shaped intraerythrocytic inclusions. The vector responsible for this patient's current condition can also transmit which of the following organisms?

- A. *Borrelia burgdorferi* (75%)
- B. Dengue virus (5%)
- C. *Haemophilus influenzae* (1%)
- D. *Histoplasma capsulatum* (2%)
- E. *Neisseria meningitidis* (0%)
- F. *Plasmodium falciparum* (14%)

Correct

75%
43 secs
03/10/2021

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This patient with an acute febrile illness, thrombocytopenia, hemolytic anemia (indirect hyperbilirubinemia, elevated lactate dehydrogenase, low haptoglobin), abnormal liver function tests, and intraerythrocytic inclusions (ring-shaped and "Maltese cross" forms) has babesiosis, a tick-borne infection. A definitive diagnosis can be made from a Giemsa-stained blood smear showing intraerythrocytic parasites. Splenectomy places patients at increased risk for severe babesiosis, which can manifest as acute respiratory distress syndrome (dyspnea, coarse crackles, bilateral infiltrates on chest x-ray).

Babesiosis (caused by *Babesia microti*) and **Lyme disease** (caused by *Borrelia burgdorferi*) are both transmitted by the *Ixodes* **tick** and occur in similar geographic regions. **Coinfection** is common and could be considered in the appropriate epidemiologic setting (eg, patients who present with babesiosis in a region endemic for Lyme disease and who do not improve despite appropriate treatment).

(Choices B and F) Dengue virus is transmitted by *Aedes* mosquitos, and *Plasmodium falciparum* is transmitted by *Anopheles* mosquitos. Dengue fever and malaria may present as acute febrile illnesses, but both infections occur mainly in tropical regions. Malaria is characterized by intravascular hemolysis, anemia, and abnormal liver function tests (similar to babesiosis), but the blood smear frequently shows ring-shaped (not cross-shaped) erythrocyte inclusions.

(Choices C and E) Asplenic patients are at increased risk for life-threatening infections with encapsulated

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Babesiosis	
Epidemiology	• Agent: *Babesia microti* • Vector: *Ixodes scapularis* **tick** (same for Lyme disease & HGA) • Geographic distribution: Northeastern United States
Clinical manifestations	• Signs & symptoms: Fevers, fatigue, myalgias, headache, **flulike symptoms** (if **severe**: ARDS, CHF, DIC, splenic rupture) • Laboratory studies: **Anemia, thrombocytopenia**, ↑LFTs
Diagnosis	• Thin blood smear (Wright/Giemsa stains): **Intraerythrocytic** pleomorphic **ring forms** (occasional "Maltese crosses")

ARDS = acute respiratory distress syndrome; **CHF** = congestive heart failure; **DIC** = disseminated intravascular coagulation; **HGA** = human granulocytic anaplasmosis; **LFTs** = liver function tests.

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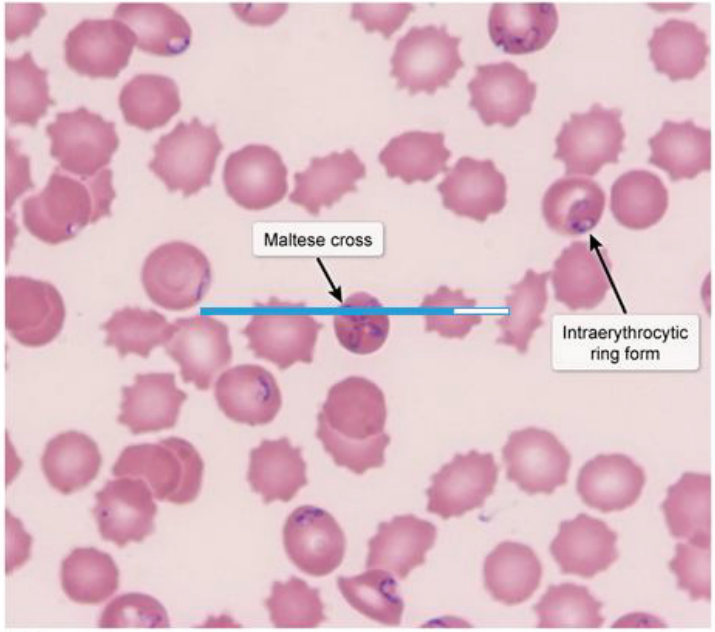
(Choices C and E) Asplenic patients are at increased risk for life-threatening infections with encapsulated

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Exhibit Display

Babesia



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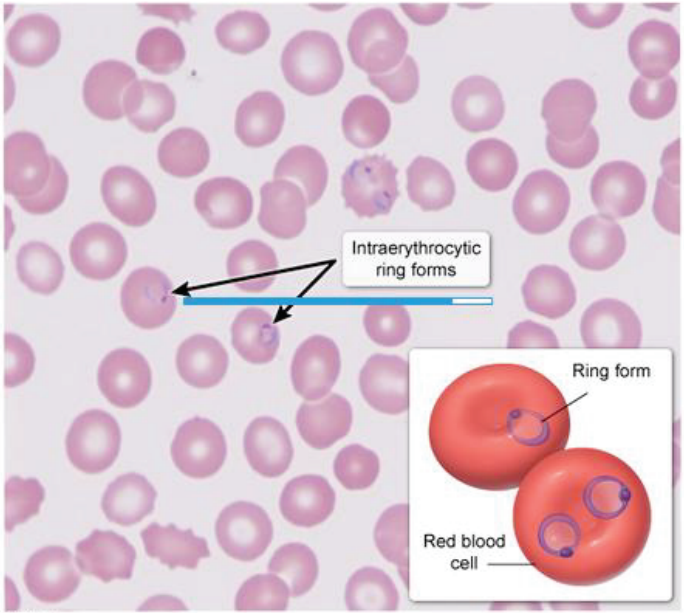
(Choices C and E) Asplenic patients are at increased risk for life-threatening infections with encapsulated

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Exhibit Display

Plasmodium



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(Choices C and E) Asplenic patients are at increased risk for life-threatening infections with encapsulated

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transmitted by *Anopheles* mosquitos. Dengue fever and malaria may present as acute febrile illnesses, but both infections occur mainly in tropical regions. Malaria is characterized by intravascular hemolysis, anemia, and abnormal liver function tests (similar to babesiosis), but the blood smear frequently shows ring-shaped (not cross-shaped) erythrocyte inclusions.

(Choices C and E) Asplenic patients are at increased risk for life-threatening infections with encapsulated organisms (eg, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*) and therefore receive protective vaccines. Intraerythrocytic inclusions are also not seen in *H influenzae* and *N meningitidis* infections.

(Choice D) Histoplasmosis is a common mycotic infection that is most commonly found in the Ohio and Mississippi river basins and is associated with activities involving exposure to bird or bat droppings (eg, caving).

Educational objective:
Babesiosis and Lyme disease are transmitted by the *Ixodes* tick and occur in similar geographic regions. Coinfection is common.

References

- Coinfections acquired from Ixodes ticks.

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A 23-year-old man comes to the emergency department with fever, severe headache, and vomiting. He has not felt well for the past 2 weeks due to fatigue, intermittent low-grade fevers, and headaches. The patient is HIV positive and spent several months in prison 3 years ago. Temperature is 38.6 C (101.5 F). Neck stiffness is present on physical examination. A CT scan reveals no intracranial lesions. Cerebrospinal fluid analysis is notable for the following:

Glucose	24 mg/dL
Protein	180 mg/dL
Leukocytes	120/mm^3

Cerebrospinal fluid cultures grow *Mycobacterium tuberculosis* with significantly decreased activity of intracellular catalase peroxidase. The isolates would most likely exhibit resistance to which of the following agents?

A. Ethambutol
B. Isoniazid

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Glucose	24 mg/dL
Protein	180 mg/dL
Leukocytes	120/mm^3

Cerebrospinal fluid cultures grow *Mycobacterium tuberculosis* with significantly decreased activity of intracellular catalase peroxidase. The isolates would most likely exhibit resistance to which of the following agents?

A. Ethambutol
B. Isoniazid
C. Pyrazinamide
D. Rifampin
E. Streptomycin

Submit

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Glucose	24 mg/dL
Protein	180 mg/dL
Leukocytes	120/mm^3

Cerebrospinal fluid cultures grow *Mycobacterium tuberculosis* with significantly decreased activity of intracellular catalase peroxidase. The isolates would most likely exhibit resistance to which of the following agents?

A. Ethambutol (8%)
B. Isoniazid (56%)
C. Pyrazinamide (11%)
D. ~~Rifampin~~ (10%)
E. ~~Streptomycin~~ (13%)

Incorrect
Correct answer

56%
06 mins, 19 secs
11/14/2020

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This patient with HIV now has headaches, fevers, and cerebrospinal fluid cultures growing *Mycobacterium tuberculosis*; this presentation is consistent with **tuberculous meningitis**.

The mechanism of action of **isoniazid** (INH) is the inhibition of mycolic acid synthesis by *M tuberculosis*. INH accomplishes this through an incompletely understood method. However, it is known that INH must be processed by **mycobacterial catalase peroxidase** for the drug to be activated within the bacteria, and that INH requires a specific protein sequence in its enzyme target (necessary for mycolic acid synthesis). For this reason, mycobacterial resistance to INH could be accomplished through non-expression of the catalase-peroxidase enzyme or through genetic modification of the INH binding site on the mycolic acid synthesis enzyme.

(Choice A) Ethambutol appears to inhibit synthesis of the mycobacterial cell wall. Resistance to this drug develops when the mycobacteria increase production of arabinosyl transferase (an enzyme in the pathway to arabinogalactan, one of the key constituents of the mycobacterial cell wall).

(Choice C) Because pyrazinamide must be converted to an active form by the mycobacterial enzyme pyrazinamidase, drug resistance can occur in those organisms that have modified their pyrazinamidase to be structurally ineffective.

(Choice D) Resistance to rifampin in *M tuberculosis* is primarily due to a mutation in the gene that codes

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to arabinogalactan, one of the key constituents of the mycobacterial cell wall).

(Choice C) Because pyrazinamide must be converted to an active form by the mycobacterial enzyme pyrazinamidase, drug resistance can occur in those organisms that have modified their pyrazinamidase to be structurally ineffective.

(Choice D) Resistance to rifampin in *M tuberculosis* is primarily due to a mutation in the gene that codes for a DNA-dependent RNA polymerase necessary for transcription and RNA prolongation.

(Choice E) Streptomycin (used in some cases of tuberculosis) is an aminoglycoside that inhibits mycobacterial protein synthesis by disabling the bacterial ribosomal 30S subunit (which disrupts translation). Resistance to this drug is primarily achieved by a modification of the 30S ribosomal protein.

Educational objective:
Mycobacterial resistance to isoniazid (INH) can be accomplished through non-expression of the catalase-peroxidase enzyme or through genetic modification of the INH binding site on the mycolic acid synthesis enzyme.

Microbiology	Infectious Diseases	Tuberculosis
Subject	System	Topic

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A previously healthy 2-year-old boy is brought to the clinic with fever and mouth pain that began yesterday. He has consumed an adequate amount of fluids but refuses to eat due to the pain. The patient has no medical problems and takes no medications. Physical examination reveals swollen gums and vesicular, inflamed lesions on his hard palate and lips. He has enlarged and tender cervical lymph nodes. Which of the following is most likely responsible for this patient's condition?

A. DNA virus, double-stranded, enveloped
B. DNA virus, double-stranded, non-enveloped
C. DNA virus, single-stranded, non-enveloped
D. RNA virus, double-stranded, positive-sense
E. RNA virus, single-stranded, negative-sense
F. RNA virus, single-stranded, positive-sense

Submit

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A previously healthy 2-year-old boy is brought to the clinic with fever and mouth pain that began yesterday. He has consumed an adequate amount of fluids but refuses to eat due to the pain. The patient has no medical problems and takes no medications. Physical examination reveals swollen gums and vesicular, inflamed lesions on his hard palate and lips. He has enlarged and tender cervical lymph nodes. Which of the following is most likely responsible for this patient's condition?

- A. DNA virus, double-stranded, enveloped (56%)
- B. DNA virus, double-stranded, non-enveloped (12%)
- C. DNA virus, single-stranded, non-enveloped (5%)
- D. ~~RNA virus, double-stranded, positive-sense~~ (3%)
- E. ~~RNA virus, single-stranded, negative-sense~~ (9%)
- F. ~~RNA virus, single-stranded, positive-sense~~ (12%)

Correct

56% Answered correctly

01 min, 15 secs Time Spent

12/14/2020 Last Updated

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Double-stranded DNA viruses	
Enveloped	• Hepadna (eg, hepatitis B) • Herpes (eg, varicella, HSV-1 & HSV-2) • Pox (eg, smallpox)
Non-enveloped	• Adenovirus • Papova (eg, HPV) • Polyoma (eg, JC & BK)

HPV= human papillomavirus; **HSV**= herpes simplex virus.

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Primary **herpes simplex virus type 1** (HSV-1) infection is characterized by the **gingivostomatitis** (vesicles on the lips and hard palate, fever, lymphadenopathy) seen in this young patient. Recurrent HSV-1 infection causes lip lesions that are typically less severe due to existing cellular and humoral immunity from prior infection.

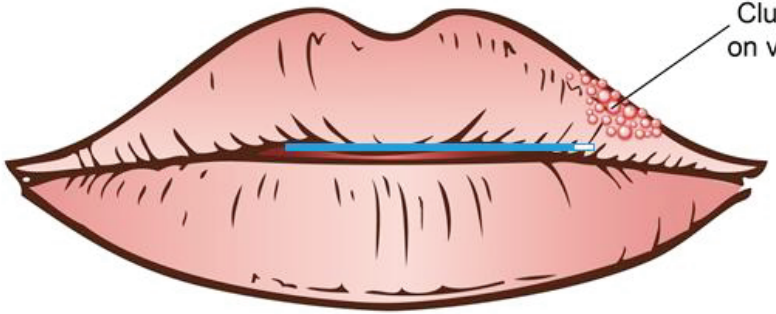
HSV-1 and other herpesviruses are **enveloped** and possess **double-stranded DNA** genomes. Transmission is usually by direct contact with infected oral secretions or lesions. Inoculation occurs on mucosa or skin where the virus replicates rapidly in the host cell nucleus and causes abnormal cell division,

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Herpes simplex virus ("cold sore")



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prior infection.

HSV-1 and other herpesviruses are **enveloped** and possess **double-stranded DNA** genomes. Transmission is usually by direct contact with infected oral secretions or lesions. Inoculation occurs on mucosa or skin where the virus replicates rapidly in the host cell nucleus and causes abnormal cell division, resulting in intranuclear inclusion bodies and **multinucleated giant cells** visible on Tzanck smear. The vesicular lesions result from cell lysis and necrosis as well as tissue destruction, inflammation, and fluid accumulation between the dermis and epidermis.

(Choice B) Most DNA viruses are double-stranded. They are enveloped (ie, surrounded by a lipid layer) or non-enveloped (ie, lacking a surrounding lipid layer). Adenovirus is a non-enveloped, double-stranded DNA virus that typically causes self-limited upper respiratory infection or gastroenteritis.

(Choice C) Parvovirus is a single-stranded, non-enveloped DNA virus that causes erythema infectiosum, or fifth disease. Patients classically present with fever, cough, and rhinorrhea followed by a "slapped-cheek" and lacy, reticular truncal rash.

(Choice D) Rotavirus, a type of reovirus, is a double-stranded, positive-sense, non-enveloped RNA virus. Rotavirus infection is a vaccine-preventable disease characterized by profuse, watery diarrhea in children.

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(Choice D) Rotavirus, a type of reovirus, is a double-stranded, positive-sense, non-enveloped RNA virus. Rotavirus infection is a vaccine-preventable disease characterized by profuse, watery diarrhea in children.

(Choices E and F) Most RNA viruses are single-stranded and can be classified as negative- or positive-sense viruses. Positive-sense viruses can be directly translated into proteins, but negative-sense stranded viruses must first have their RNA converted into positive-sense strands before translation. Coxsackievirus, a single-stranded, positive-sense RNA virus of the enterovirus family, causes hand, foot, and mouth disease, which presents with vesicular lesions on the buccal mucosa, tongue, and soft palate. The gums and hard palate are usually involved in HSV gingivostomatitis, not hand-foot-mouth disease.

Educational objective:

Primary herpes simplex virus type 1 (HSV-1) infection in children causes gingivostomatitis (vesicular lesions on the lips and hard palate). HSV-1 and other herpesviruses are double-stranded, enveloped DNA viruses.

References

- The RNA synthesis machinery of negative-stranded RNA viruses.
- Ultrastructure of the replication site of positive-stranded RNA viruses.

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Single-stranded RNA viruses	
Negative-sense	• Arena (eg, Lassa) • Bunya (eg, hantavirus) • Delta (eg, hepatitis D) • Filo (eg, Ebola, Marburg) • Orthomyxo (eg, influenza) • Paramyxo (eg, RSV, mumps, measles) • Rhabdo (eg, rabies)
Positive-sense	• Calici (eg, norovirus) • Corona (eg, SARS) • Flavi (eg, West Nile, hepatitis C, dengue, yellow fever) • Hepe (eg, hepatitis E virus) • Picorna (eg, hepatitis A, enteroviruses) • Retro (eg, HIV) • Toga (eg, rubella)

RSV= respiratory syncytial virus; **SARS**= severe acute respiratory syndrome.

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Hand foot and mouth disease Hand foot and mouth



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Exhibit Display

Hand foot and mouth disease Hand foot and mouth



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A 22-year-old man who recently immigrated to the United States comes to the physician for routine care. He has no current symptoms. He takes no medications and has no known allergies. Laboratory testing yields the following results:

Anti-hepatitis A IgM	Negative
Anti-hepatitis A IgG	Positive

The patient's country of origin does not offer universal immunization against hepatitis A, and he says he has not been vaccinated against the virus. Which of the following do these laboratory findings most likely suggest?

A. Anicteric viral infection as a toddler
B. Asymptomatic viral carrier state
C. Chronic viral hepatitis

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The patient's country of origin does not offer universal immunization against hepatitis A, and he says he has not been vaccinated against the virus. Which of the following do these laboratory findings most likely suggest?

A. Anicteric viral infection as a toddler
B. Asymptomatic viral carrier state
C. Chronic viral hepatitis
D. Immunity against hepatitis D infection
E. Liver failure during childhood
F. Occult cirrhosis
G. Reinfection with hepatitis A virus
H. Window period

Submit

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The patient's country of origin does not offer universal immunization against hepatitis A, and he says he has not been vaccinated against the virus. Which of the following do these laboratory findings most likely suggest?

- A. Anicteric viral infection as a toddler (72%)
- B. Asymptomatic viral carrier state (13%)
- C. Chronic viral hepatitis (5%)
- D. Immunity against hepatitis D infection (1%)
- E. Liver failure during childhood (0%)
- F. Occult cirrhosis (0%)
- G. Reinfection with hepatitis A virus (4%)
- H. Window period (2%)

Correct

72%
Answered correctly

59 secs
Time Spent

09/28/2020
Last Updated

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This asymptomatic patient with immunoglobulin G (IgG) antibodies against **hepatitis A virus** (HAV) likely had a prior infection with HAV. In children age <6, HAV infection is most often (>80%) silent or subclinical ("**anicteric**," with no jaundice observed). Less frequently, it can present as an acute, self-limited illness characterized by jaundice, malaise, fatigue, anorexia, nausea, vomiting, and right upper-quadrant pain. Clinical disease is typically more severe (70% of symptomatic patients with jaundice) in adults (some of whom develop an aversion to smoking, for unclear reasons), although in the United States most adults with anti-HAV IgG antibodies have never experienced an icteric illness. Liver failure and death due to HAV are extremely rare (<0.5% of cases) **(Choice E)**.

(Choices B, C, and F) Unlike hepatitis B or C, HAV infection is a self-limiting disease that is not associated with an asymptomatic viral carrier state and does not progress to chronic hepatitis, cirrhosis, or hepatocellular carcinoma.

(Choice D) Immunity against hepatitis D virus (HDV) infection would be signaled by anti-HDV IgG antibodies, not anti-HAV IgG antibodies.

(Choice G) Reinfection with HAV would be associated with the presence of anti-HAV IgM antibodies. Individuals who have persistent anti-HAV IgG antibodies typically enjoy immunity to repeat HAV infection.

(Choice H) Acute hepatitis B infection is sometimes associated with a window period where hepatitis B

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(Choice D) Immunity against hepatitis D virus (HDV) infection would be signaled by anti-HDV IgG antibodies, not anti-HAV IgG antibodies.

(Choice G) Reinfection with HAV would be associated with the presence of anti-HAV IgM antibodies. Individuals who have persistent anti-HAV IgG antibodies typically enjoy immunity to repeat HAV infection.

(Choice H) Acute hepatitis B infection is sometimes associated with a window period where hepatitis B surface antigen (HBsAg) is no longer present but anti-HBsAg is not yet detectable in serum.

Educational objective:

Hepatitis A virus infection is most commonly silent or subclinical ("anicteric") in young children but can also present as an acute, self-limited illness characterized by jaundice, malaise, fatigue, anorexia, nausea, vomiting, right upper-quadrant pain, or an aversion to smoking.

References

- Hepatitis A: epidemiology and prevention in developing countries.

Microbiology	Infectious Diseases	Hepatitis a
Subject	System	Topic

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An 83-year-old man comes to the emergency department due to a 1-week history of fever, malaise, cough, right-sided chest pain, and worsening dyspnea. Temperature is 38.4 C (101.1 F), blood pressure is 116/70 mm Hg, and pulse is 98/min. On physical examination, the patient is frail appearing. Breath sounds are decreased on the right side. Heart sounds are normal. The abdomen is soft and nontender. Chest x-ray shows a moderate-sized right pleural effusion. Thoracentesis yields purulent fluid. Pleural fluid analysis reveals a large number of leukocytes with 80% neutrophils. Which of the following is the most likely underlying mechanism for this patient's pleural effusion?

A. Bacterial translocation from alveoli into pleural space
B. Contiguous spread from a mediastinal focus
C. Direct inoculation into the pleural space
D. Hematogenous dissemination of a distant infection
E. Reactivation of a dormant infection

Submit

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An 83-year-old man comes to the emergency department due to a 1-week history of fever, malaise, cough, right-sided chest pain, and worsening dyspnea. Temperature is 38.4 C (101.1 F), blood pressure is 116/70 mm Hg, and pulse is 98/min. On physical examination, the patient is frail appearing. Breath sounds are decreased on the right side. Heart sounds are normal. The abdomen is soft and nontender. Chest x-ray shows a moderate-sized right pleural effusion. Thoracentesis yields purulent fluid. Pleural fluid analysis reveals a large number of leukocytes with 80% neutrophils. Which of the following is the most likely underlying mechanism for this patient's pleural effusion?

- A. Bacterial translocation from alveoli into pleural space (68%)
- B. Contiguous spread from a mediastinal focus (7%)
- C. ~~Direct inoculation into the pleural space~~ (9%)
- D. ~~Hematogenous dissemination of a distant infection~~ (9%)
- E. ~~Reactivation of a dormant infection~~ (5%)

68% 02 mins, 03 secs 11/06/2020

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Parapneumonic effusions		
	Uncomplicated	**Complicated***
Etiology	Sterile exudate in pleural space	Bacterial invasion of pleural space
Radiologic appearance	Small to moderate & free flowing	Moderate to large, free flowing or loculated
Pleural fluid characteristics	• pH ≥7.2 • Glucose ≥60 mg/dL • WBCs ≤50,000/mm^3	• pH <7.2 • Glucose <60 mg/dL • WBCs >50,000/mm^3
Treatment	Antibiotics	Antibiotics + drainage
*Empyema represents advanced progression of a complicated		

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*Empyema represents advanced progression of a complicated effusion.
WBC = white blood cell.

Thoracentesis yielding **purulent fluid** is diagnostic of **empyema**, a pleural effusion that has been contaminated by bacteria (or, rarely, fungi or parasites) with subsequent inflammatory progression and fibrotic organization within the pleural space (often with loculated fluid collections). Empyema most commonly results from **bacterial translocation from the alveoli into the pleural space** and represents advanced progression of a complicated parapneumonic effusion. Affected patients have a symptomatic presentation similar to that of pneumonia (eg, fever, cough, shortness of breath, pleuritic chest pain), but the presentation can be more insidious than uncomplicated pneumonia, taking place over 1-2 weeks or more.

Treatment of empyema requires prompt drainage (eg, chest tube, surgery in some cases) in additon to antibiotics. Following drainage, some patients have persistent pleural fibrosis that prevents full lung reexpansion, a complication known as trapped lung.

(Choices B, C, D, and E) Contiguous spread from a mediastinal focus, direct inoculation (eg, surgery, penetrating trauma), hematogenous dissemination of a distant infection, and reactivation of a dormant

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(Choices B, C, D, and E) Contiguous spread from a mediastinal focus, direct inoculation (eg, surgery, penetrating trauma), hematogenous dissemination of a distant infection, and reactivation of a dormant infection (eg, tuberculosis) are all possible but less common etiologies of bacterial contamination of the pleural space leading to empyema. In the absence of evidence that suggests one of these sources (eg, recent surgery or trauma, lymphocyte-predominant effusion consistent with tuberculosis), empyema in this patient is most likely due to bacterial translocation from the alveoli (a complication of pneumonia).

Educational objective:

Empyema is an accumulation of pus within the pleural space that can result from multiple sources of bacterial contamination. It usually represents advanced progression of a complicated parapneumonic effusion resulting from bacterial translocation from the alveoli.

References

- Empyema.

Microbiology	Infectious Diseases	Parapneumonic effusion & Empyema
Subject	System	Topic

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A 24-year-old man comes to the physician with painful blisters on the shaft of his penis. The lesions erupted 2 days ago. The patient has had 5 lifetime sexual partners and is currently sexually active with one female partner; he uses condoms inconsistently. Examination shows multiple vesicular lesions on the penis, and Tzanck smear is positive for multinucleated giant cells. HIV testing is negative. The patient has had several similar episodes every year for the past 2 years but had been too embarrassed to seek treatment until now. Which of the following would most likely have prevented recurrence of this patient's condition?

A. Continuous daily valacyclovir
B. Immunoglobulin during the first episode
C. Lamivudine with recurrence of blisters
D. Regular condom use after the first episode
E. Weeklong course of acyclovir during the first episode

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A 24-year-old man comes to the physician with painful blisters on the shaft of his penis. The lesions erupted 2 days ago. The patient has had 5 lifetime sexual partners and is currently sexually active with one female partner; he uses condoms inconsistently. Examination shows multiple vesicular lesions on the penis, and Tzanck smear is positive for multinucleated giant cells. HIV testing is negative. The patient has had several similar episodes every year for the past 2 years but had been too embarrassed to seek treatment until now. Which of the following would most likely have prevented recurrence of this patient's condition?

- A. Continuous daily valacyclovir (52%)
- B. Immunoglobulin during the first episode (1%)
- C. Lamivudine with recurrence of blisters (2%)
- D. Regular condom use after the first episode (6%)
- E. Weeklong course of acyclovir during the first episode (37%)

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This patient's recurrent vesicular lesions and positive Tzanck smear are consistent with recurrent **genital herpes simplex virus (HSV)**, generally due to reactivation of latent HSV-2 infection within the S2, S3, and S4 dorsal root (sensory) ganglia. Recurrence of genital HSV can be suppressed or minimized with daily oral valacyclovir (preferred as it is dosed once daily and has good bioavailability), acyclovir, or famciclovir. Although the antiviral agents may not be active against latent virus forms, they can suppress further multiplication as soon as reactivation occurs. Suppressive therapy would likely have been offered to this patient with multiple yearly episodes of recurrence; it is generally continued for years with periodic re-evaluation.

(Choice B) Immunoglobulin therapy can be used for varicella postexposure prophylaxis (eg, in neonates or pregnant women) but is not commonly used for genital HSV infections.

(Choice C) Lamivudine is a nucleoside analog reverse transcriptase inhibitor with activity against HIV and hepatitis B virus. It is not known to be effective against HSV-2.

(Choice D) Although condom use may prevent sexual transmission of HSV-2 (and therefore might have prevented this patient from acquiring his primary genital HSV-2 infection), it does not reduce the frequency of recurrence of genital herpes.

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hepatitis B virus. It is not known to be effective against HSV-2.

(Choice D) Although condom use may prevent sexual transmission of HSV-2 (and therefore might have prevented this patient from acquiring his primary genital HSV-2 infection), it does not reduce the frequency of recurrence of genital herpes.

(Choice E) A short (7-10 days) course of treatment with oral acyclovir during primary genital HSV infection usually reduces the duration of viral shedding, time for lesional healing, and local pain; however, it does not appear to alter recurrence rates.

Educational objective:

A new-onset genital vesicular rash with a positive Tzanck smear in a previously asymptomatic patient is suggestive of primary genital herpes simplex virus (HSV) infection due to HSV-2. Recurrences of genital herpes can be reduced through daily treatment with oral valacyclovir, acyclovir, or famciclovir. Condom use can help prevent a primary genital HSV infection but does not prevent reactivation of latent infection.

References

- Genital herpes.

Microbiology Infectious Diseases HSV infection

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A 38-year-old woman who works as a nurse at a large community hospital is undergoing evaluation following an accidental needlestick in the operating room. The patient being operated on is not known to have any infections. As part of her evaluation, the nurse has serologic testing for viral hepatitis. Laboratory results are as follows:

Anti-HAV IgM	negative
Anti-HAV IgG	positive
HBsAg	negative
HBeAg	negative
Anti-HBs	positive
Anti-HBc IgM	negative
Anti-HBc IgG	negative
Anti-HBe	negative
Anti-HCV	negative

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Anti-HBs	positive
Anti-HBc IgM	negative
Anti-HBc IgG	negative
Anti-HBe	negative
Anti-HCV	negative

Which of the following statements is most likely to be true regarding the nurse's viral status?

A. She has been vaccinated against hepatitis B virus (HBV)
B. She has chronic hepatitis but is non-contagious
C. She has recovered from HBV infection recently
D. She is actively shedding hepatitis A virus
E. She is an asymptomatic carrier of HBV
F. She is infected with hepatitis D virus

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Anti-HBc IgG	negative
Anti-HBe	negative
Anti-HCV	negative

Which of the following statements is most likely to be true regarding the nurse's viral status?

- A. She has been vaccinated against hepatitis B virus (HBV) (88%)
- B. She has chronic hepatitis but is non-contagious (1%)
- C. She has recovered from HBV infection recently (3%)
- D. She is actively shedding hepatitis A virus (1%)
- E. She is an asymptomatic carrier of HBV (3%)
- F. She is infected with hepatitis D virus (0%)

Correct

88%

27 secs

12/03/2020

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Importance of hepatitis B serological markers	
HBsAg	• HBV surface glycoproteins • Detectable during acute infection • Persistence >6 months = **chronic infection**
HBeAg	• HBV polypeptide • Detectable during acute infection • Indicates ↑ **viral replication** & infectivity
Anti-HBc IgM	• First sign of **acute** infection • Present during **window phase** prior to HBsAg & HBeAg
Anti-HBs	• Seen with cleared infection or vaccination • Confers long-term **immunity**
Anti-HBe	• Develops in cleared infection & later in chronic infection • Indicates ↓ **viral replication** & infectivity
Anti-HBc IgG	• Present in both acute & chronic infection

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Anti-HBc IgG	• Present in both acute & chronic infection • **Not present** after vaccination

This patient's laboratory studies are typical of **hepatitis B vaccination**. The hepatitis B vaccine is a safe and highly effective recombinant vaccine that contains HBsAg, a surface antigen that stimulates the production of anti-HBs in the host. **Anti-HBs** is a **neutralizing antibody** that prevents viral entry into cells. Therefore, individuals who receive the vaccination will develop immunity and be positive for anti-HBs but **negative for HBsAg**.

In contrast to the vaccine, which only contains HBsAg, infection with hepatitis B virus (HBV) exposes patients to additional antigens. Hepatitis B core antigen (HBcAg) is found within the virus and on infected hepatocytes but does not circulate in the bloodstream. If this patient had actually experienced HBV infection, her **anti-HBc** would also be positive **(Choice C)**. Hepatitis B e antigen (HBeAg) is involved in viral replication, and detection of **HBeAg** in the bloodstream implies high levels of viral replication and infectivity.

(Choices B and E) Persistence of HBsAg in the bloodstream indicates chronic hepatitis. Patients with no circulating HBeAg, presence of anti-HBe, and low viral loads have a lower risk of disease progression and are less likely to transmit HBV.

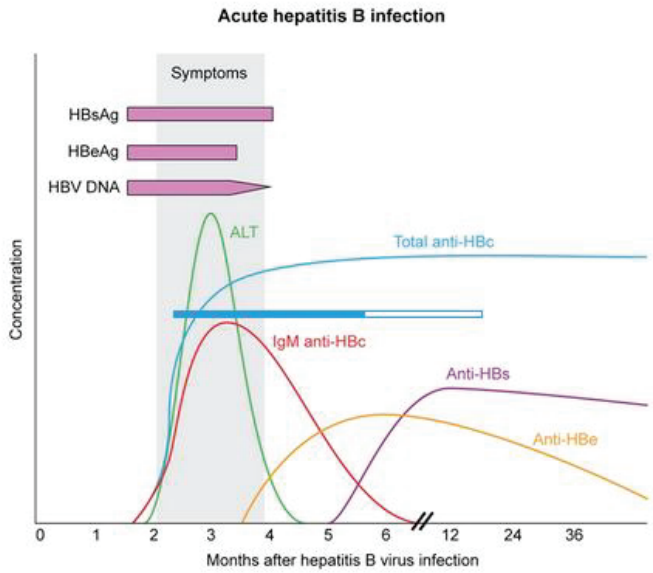
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Present in both acute & chronic infection

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Acute and chronic hepatitis B infection Acute and chronic hepatitis B infection



ALT = alanine aminotransferase; **anti-HBc** = hepatitis B core antibody; **anti-HBe** = hepatitis B e antibody; **anti-HBs** = hepatitis B surface antibody; **HBeAg** = hepatitis B e antigen; **HBsAg** = hepatitis B surface antigen; **HBV** = hepatitis B virus.

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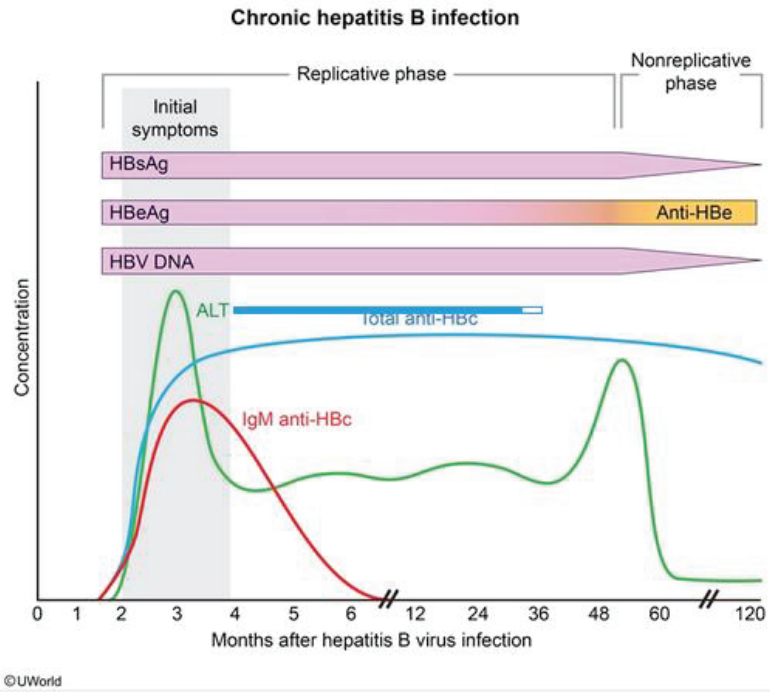
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Exhibit Display

Acute and chronic hepatitis B infection Acute and chronic hepatitis B infection



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circulating HBeAg, presence of anti-HBe, and low viral loads have a lower risk of disease progression and are less likely to transmit HBV.

(Choice D) The presence of anti-hepatitis A virus (HAV) IgG suggests that this patient is protected from acute HAV infection. It is impossible to determine from the information given whether the anti-HAV IgG is due to previous infection or immunization with the hepatitis A vaccine.

(Choice F) The hepatitis D virus (HDV) is replication defective and depends on the genetic information provided by HBV for replication. This individual is not infected with HBV (her HBsAg is negative) and therefore cannot be infected with HDV.

Educational objective:
Individuals who are successfully immunized against hepatitis B virus develop protective anti-HBs antibody. Individuals who recover from hepatitis B infection, however, have anti-HBs as well as anti-HBc antibodies. The presence of circulating HBsAg indicates active infection.

Microbiology	Infectious Diseases	Hepatitis b
Subject	System	Topic

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A 21-year-old woman volunteers in a research study evaluating the effects of viral infection on immunoglobulin production. The patient is a college student who has no past medical history and does not take any medications. She has not felt ill recently. Her lymphocytes are isolated from whole blood and cultured. The mature B lymphocytes exposed to a specific virus *in vitro* acquire the ability to proliferate indefinitely while maintaining the capacity to secrete immunoglobulins. Which of the following tests is used to diagnose an *in vivo* infection with this virus?

A. Circulating surface antigen
B. Cryoglobulins
C. Hemadsorption in the cell culture
D. Heterophile antibodies
E. Papanicolaou test
F. Tzanck smear

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A. Circulating surface antigen (12%)
B. Cryoglobulins (5%)
C. Hemadsorption in the cell culture (1%)
D. Heterophile antibodies (67%)
E. Papanicolaou test (5%)
F. Tzanck smear (7%)

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Epstein-Barr virus (EBV) commonly infects B cells, stimulating them to enter the cell cycle and proliferate continuously ("transformation" or "**immortalization**"). This is accomplished when EBV-encoded oncogenes activate proliferative and anti-apoptotic signaling pathways within the infected B cell. In an immunocompetent host, a vigorous immune response holds EBV-induced B cell proliferation in check. The immortalized B cells maintain the ability to **secrete immunoglobulins** (Ig) and B-cell activation products (eg, CD23), with very few of them releasing virus particles at any one time.

Diagnosing EBV infection relies on detecting a heterogeneous group of **heterophile** IgM **antibodies** that react with antigens on horse erythrocytes (or sheep erythrocytes in the classic Paul Bunnell test). Agglutination of these horse erythrocytes by human serum is a sensitive and highly specific (~100%) test for EBV infection in human B cells. The mechanism remains unclear; EBV either induces a humoral response to heterophile antigens or stimulates nonspecific polyclonal activation of B cells.

(Choice A) EBV typically causes a latent infection of B cells, with viral genome persistence but no full virion replication, no lytic release, and sparse viral protein expression. Normally, only minimal amounts of EBV-specific antigens circulate in an immunocompetent host; therefore, blood tests for such antigens are insensitive to latent EBV infection. Detection of circulating surface antigen is used to diagnose hepatitis B

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virion replication, no lytic release, and sparse viral protein expression. Normally, only minimal amounts of EBV-specific antigens circulate in an immunocompetent host; therefore, blood tests for such antigens are insensitive to latent EBV infection. Detection of circulating surface antigen is used to diagnose hepatitis B virus infection.

(Choice B) Cryoglobulins, cold-precipitable serum proteins that contain Igs, are most commonly associated with hepatitis C virus infection.

(Choice C) Some influenza and parainfluenza viruses are associated with hemadsorption (hemagglutinins or glycoproteins with a high affinity for erythrocytes expressed on the host cell surface). Hemadsorption is not characteristic of EBV.

(Choice E) The Papanicolaou test is used to screen cervical cytology specimens for dysplasia caused by oncogenic strains of human papillomavirus.

(Choice F) Tzanck smear is used to diagnose herpes simplex or varicella zoster virus infection. The epithelial cells scraped from the ulcer base are prepared with a Wright-Giemsa stain and examined for multinucleated giant cells and intranuclear inclusions.

Educational objective:
Epstein-Barr virus (EBV) commonly infects B cells, stimulating them to proliferate continuously

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Educational objective:
Epstein-Barr virus (EBV) commonly infects B cells, stimulating them to proliferate continuously ("transformation" or "immortalization"). EBV is an oncogenic virus that promotes polyclonal B cell proliferation and heterophile antibody production. The heterophile antibody test is sensitive and highly specific for EBV infection.

Microbiology	Infectious Diseases	Infectious mononucleosis
Subject	System	Topic

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A 56-year-old man comes to the office due to several months of progressive neck swelling. He has also had intermittent epistaxis and headaches. The patient has no chronic medical conditions and takes no medications. He does not use tobacco, alcohol, or illicit drugs, and he emigrated to the United States from rural China 12 years ago. Physical examination shows several enlarged, firm, and nontender cervical lymph nodes. Nasopharyngeal evaluation reveals a mass arising from the pharyngeal recess. Histopathological examination of the mass shows undifferentiated malignant cells of epithelial origin. Further analysis of these cells is most likely to reveal the presence of nucleic acid sequences from which of the following viruses?

- A. Adenovirus
- B. Coronavirus
- C. Cytomegalovirus
- D. Epstein-Barr virus
- E. Human herpes virus 8
- F. Polyomavirus

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medications. He does not use tobacco, alcohol, or illicit drugs, and he emigrated to the United States from rural China 12 years ago. Physical examination shows several enlarged, firm, and nontender cervical lymph nodes. Nasopharyngeal evaluation reveals a mass arising from the pharyngeal recess. Histopathological examination of the mass shows undifferentiated malignant cells of epithelial origin. Further analysis of these cells is most likely to reveal the presence of nucleic acid sequences from which of the following viruses?

A. Adenovirus (1%)
B. Coronavirus (0%)
C. Cytomegalovirus (2%)
✓ D. Epstein-Barr virus (90%)
E. Human herpes virus 8 (3%)
F. Polyomavirus (1%)

Correct
90%
57 secs
11/29/2020

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Nasopharyngeal carcinoma is an epithelial tumor that usually originates in the pharyngeal recess. Local tumor growth often leads to epistaxis and headaches, and metastatic spread to cervical lymph nodes frequently causes firm, fixed neck swelling. NPC is relatively uncommon in the United States but is endemic to **southern China**, where genetic and dietary factors (eg, consumption of salted fish) predispose to premalignant nasopharyngeal epithelial lesions. Subsequent **malignant transformation** is then induced by **Epstein-Barr virus** (EBV).

EBV is a ubiquitous human herpes virus that causes infectious mononucleosis in a minority of patients (primary infection is usually asymptomatic). Initial infection is followed by life-long **latent infection** in memory B cells. While latent, the EBV genome exists as an episome in the nucleus of infected cells and expresses a restricted subset of EBV genes (**latency genes**) which do the following:

- Promote periodic viral reactivation from memory B-cells, leading to recurrent (asymptomatic) mucosal infections.
- Promote survival of infected memory B cells by encoding for proteins (eg, EBNA-1, LMP1) that prevent apoptosis. In a minority of patients, these proteins are oncogenic and lead to **malignant transformation** of infected B cells (eg, Burkitt lymphoma, Hodgkin lymphoma) or premalignant epithelial cells (eg, nasopharyngeal carcinoma, salivary cancer).

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apoptosis. In a minority of patients, these proteins are oncogenic and lead to **malignant transformation** of infected B cells (eg, Burkitt lymphoma, Hodgkin lymphoma) or premalignant epithelial cells (eg, nasopharyngeal carcinoma, salivary cancer).

Individuals who do not have premalignant epithelial lesions are at very low risk of EBV-associated epithelial cancers like NPC.

(Choice A) Adenovirus causes acute upper respiratory infection with pharyngitis, coryza, otitis media, bronchitis, and/or pneumonia. It is not associated with nasopharyngeal carcinoma.

(Choice B) Coronavirus is one of the most common causes of upper respiratory tract infection (eg, common cold) but has no association with nasopharyngeal or other cancers.

(Choices C and E) Cytomegalovirus (CMV) and human herpes virus 8 (HHV-8) are also herpes viruses; as such, they cause acute infection followed by latent disease. Although CMV can reactivate in immunocompromised individuals (eg, HIV, post-transplantation) and cause severe end-organ disease (eg, retinitis, gastroenteritis), it is not an oncogenic virus. HHV-8 reactivation also primarily occurs in immunocompromised individuals and is associated with Kaposi sarcoma.

(Choice F) The BK and JC viruses are members of Polyomaviridae and cause life-long latent infections in the kidney. BK reactivation can cause nephropathy in renal transplant recipients, and JC virus causes

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(Choices C and E) Cytomegalovirus (CMV) and human herpes virus 8 (HHV-8) are also herpes viruses; as such, they cause acute infection followed by latent disease. Although CMV can reactivate in immunocompromised individuals (eg, HIV, post-transplantation) and cause severe end-organ disease (eg, retinitis, gastroenteritis), it is not an oncogenic virus. HHV-8 reactivation also primarily occurs in immunocompromised individuals and is associated with Kaposi sarcoma.

(Choice F) The BK and JC viruses are members of Polyomaviridae and cause life-long latent infections in the kidney. BK reactivation can cause nephropathy in renal transplant recipients, and JC virus causes progressive multifocal leukoencephalopathy (primarily in patients with advanced HIV).

Educational objective:

Nasopharyngeal cancer is endemic in southern China due to genetic and dietary factors that promote nasopharyngeal epithelial pre-malignant lesions. In almost all cases, malignant transformation occurs due to infection of premalignant cells with Epstein-Barr virus and the subsequent expression of oncogenic viral proteins.

References

- Epstein-Barr virus and nasopharyngeal carcinoma.

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www.ncbi.nlm.nih.gov/pubmed/25418193

A 10-week-old boy is brought to the office for a follow-up visit. As part of his routine immunization schedule, the patient received the first dose of the *Haemophilus influenzae* type b (Hib) conjugate vaccine when he was 8 weeks old. However, following vaccine administration, he developed anaphylaxis, requiring epinephrine administration and hospitalization. As a result, the decision was made not to administer additional doses of the Hib vaccine. The patient was born full-term by uncomplicated vaginal delivery and has otherwise been healthy. Physical examination is unremarkable. His older brother has completed the full vaccination course. This patient is at highest risk of which of the following infections compared to his brother?

A. Acute bronchiolitis
B. Bacterial conjunctivitis
C. Meningitis
D. Otitis media
E. Sinusitis

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A. Acute bronchiolitis (4%)

B. Bacterial conjunctivitis (0%)

✓ C. Meningitis (72%)

D. Otitis media (19%)

E. Sinusitis (1%)

Correct

72%

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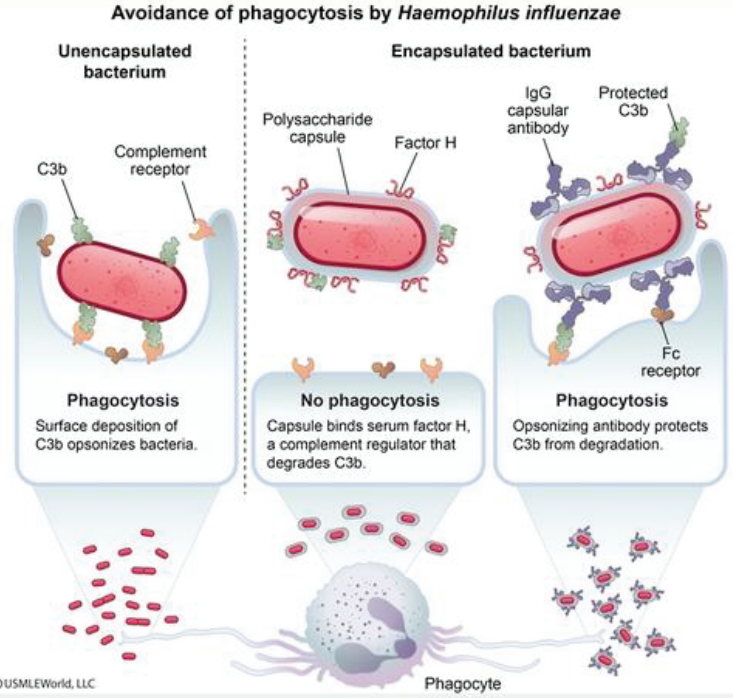
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www.ncbi.nlm.nih.gov/pubmed/25418193

Unencapsulated | Encapsulated bacterium

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Haemophilus influenzae is a gram-negative coccobacillus that can be either encapsulated (serotypes a-f) or unencapsulated (nontypeable). *H influenzae* **type b** (Hib) is the most invasive strain due to its polyribosylribitol phosphate **(PRP) capsule**, which **inhibits complement-mediated phagocytosis** and allows it to invade tissues and survive in the bloodstream.

During the first months of life, transient immunity to Hib is accomplished by IgG antibodies acquired transplacentally from the mother while in utero. The **Hib vaccine** is administered beginning at age 2 months to provide continued immunity. The immunization is composed of PRP conjugated with a protein toxoid (eg, tetanus, diphtheria), which induces a T cell–dependent immune response. The production of opsonizing anticapsular antibodies by B-lymphocytes allows for efficient phagocytosis of the bacterium. Without the protection from the vaccine, this child is at risk for **invasive disease** caused by Hib, such as **meningitis**, bacteremia, pneumonia, and epiglottitis.

(Choice A) Bronchiolitis is a lower respiratory infection that is almost always viral in etiology. Respiratory syncytial virus, rhinovirus, influenza, and parainfluenza are commonly implicated, but not *H influenzae*.

(Choices B, D, and E) Most causes of bacterial conjunctivitis, acute otitis media, and sinusitis in childhood are due to *Streptococcus pneumoniae*, nontypeable *H influenzae*, and *Moraxella catarrhalis*. The Hib vaccine (which has no effect on nontypeable *H influenzae*) will not protect a child from these infections.

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Without the protection from the vaccine, this child is at risk for **invasive disease** caused by Hib, such as **meningitis**, bacteremia, pneumonia, and epiglottitis.

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(Choices B, D, and E) Most causes of bacterial conjunctivitis, acute otitis media, and sinusitis in childhood are due to *Streptococcus pneumoniae*, nontypeable *H influenzae*, and *Moraxella catarrhalis*. The Hib vaccine (which has no effect on nontypeable *H influenzae*) will not protect a child from these infections.

Educational objective:

The *Haemophilus influenzae* type b (Hib) vaccine induces anticapsular antibodies that facilitate complement-mediated phagocytosis of the bacterium. The vaccination series has drastically reduced the incidence of invasive disease caused by Hib, such as meningitis, bacteremia, pneumonia, and epiglottitis.

References

- Pediatric invasive Haemophilus influenzae infections in Israel in the era of Haemophilus influenzae type b vaccine: a nationwide prospective study.

Microbiology	Infectious Diseases	Meningitis
Subject	System	Topic

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A 21-year-old man comes to the urgent care clinic with a lesion on his penis. He noted a painful ulcer on the right side of the penis 4 days ago and it has progressively increased in size since then. The patient has had no dysuria, hematuria, or penile discharge. He is a tourist visiting New York City from Botswana. He is HIV-positive and is sexually active. The patient currently takes no medications. He appears comfortable and is afebrile. On genitourinary examination, there is a 1.5-cm ulceration on the right side of the base of the penis; this lesion is very tender and soft; has irregular, ragged borders; and is covered with grey exudate. There is no penile discharge. There is a palpable, tender, enlarged inguinal lymph node in the right groin. The examination is otherwise unremarkable. A scraping of the ulcer is performed. Polymerase chain reaction testing for herpes simplex virus is negative, and darkfield microscopy reveals no organisms. Which of the following is the most likely diagnosis?

A. Chancroid
B. Condyloma acuminatum
C. Cytomegalovirus infection
D. Gonorrhea
E. Granuloma inguinale

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A. Chancroid
B. Condyloma acuminatum
C. Cytomegalovirus infection
D. Gonorrhea
E. Granuloma inguinale
F. Molluscum contagiosum
G. Secondary syphilis
H. Squamous cell carcinoma

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right groin. The examination is otherwise unremarkable. A scraping of the ulcer is performed. Polymerase chain reaction testing for herpes simplex virus is negative, and darkfield microscopy reveals no organisms. Which of the following is the most likely diagnosis?

- A. Chancroid (60%)
- B. ~~Condyloma acuminatum~~ (5%)
- C. Cytomegalovirus infection (2%)
- D. ~~Gonorrhea~~ (2%)
- E. Granuloma inguinale (19%)
- F. ~~Molluscum contagiosum~~ (2%)
- G. ~~Secondary syphilis~~ (2%)
- H. ~~Squamous cell carcinoma~~ (4%)

Correct

60%

02 mins, 11 secs

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Characteristics of ulcerative sexually transmitted diseases			
Disease	**Causative agent**	**Features of primary lesion**	**Initial lesion painful?**
Chancroid	*Haemophilus ducreyi*	• Multiple & deep ulcers • Base may have gray to yellow exudate • Organisms often clump in long parallel strands ("school of fish")	Yes
Genital herpes	Herpes simplex virus 1 & 2	• Multiple, small, grouped ulcers • Shallow with erythematous base • Multinucleated giant cells & intranuclear inclusions (Cowdry type A)	Yes
		• Extensive & progressive ulcerative lesions without lymphadenopathy	

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Granuloma inguinale (donovanosis)	*Klebsiella granulomatis*	• Extensive & progressive ulcerative lesions without lymphadenopathy • Base may have granulation-like tissue • Deeply staining gram-negative intracytoplasmic cysts (Donovan bodies)	No
Syphilis	*Treponema pallidum*	• Single, indurated, well-circumscribed ulcer • Nonexudative base • Painless inguinal lymphadenopathy • Thin, delicate, corkscrew-shaped organisms on dark-field microscopy	No
Lymphogranuloma	*Chlamydia*	• Small & shallow ulcers • Large, painful, coalesced inguinal lymph nodes ("buboes")	No

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Lymphogranuloma venereum	*Chlamydia trachomatis*	• Small & shallow ulcers • Large, painful, coalesced inguinal lymph nodes ("buboes") • Intracytoplasmic chlamydial inclusion bodies in epithelial cells & leukocytes	No

Chancroid is caused by ***Haemophilus ducreyi***, a gram-negative bacterium transmitted through sexual contact. It presents as one or more deep, **painful** ulcers (you "do cry" with *H ducreyi*) with **ragged borders** that are associated with a **grey exudate** and inguinal lymphadenopathy. On Gram stain, the organism appears as curved, gram-negative rods, often in a **clumping** pattern. The disease is relatively uncommon in the United States but has much higher prevalence in sub-Saharan Africa, Latin America, and regions of Asia.

(Choice B) Condyloma acuminata, or genital warts, are caused by the human papillomavirus. They present as skin-colored, white, or grey verrucous and filiform papules usually in the penile glans and shaft in men and the vulvovaginal and cervical areas in women.

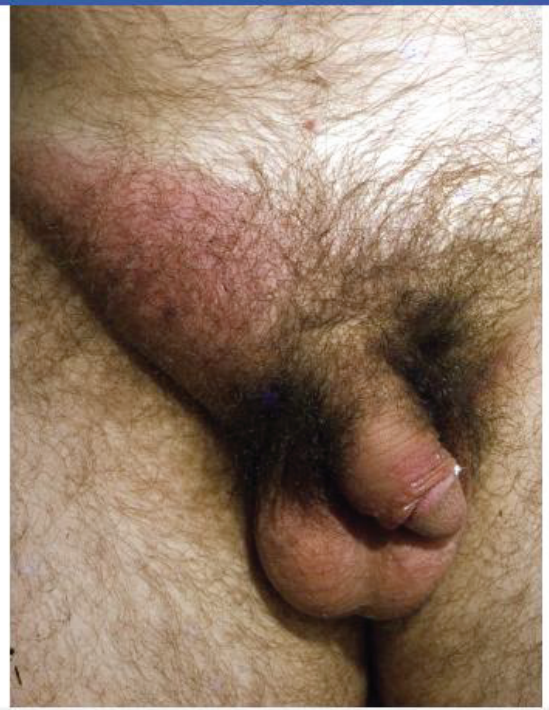
(Choice C) In immunocompromised patients, manifestations of cytomegalovirus infection include febrile illness, pneumonitis, hepatitis, and retinitis, among others.

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in men and the vulvovaginal and cervical areas in women.

(Choice C) In immunocompromised patients, manifestations of cytomegalovirus infection include febrile illness, pneumonitis, hepatitis, and retinitis, among others.

(Choice D) Gonorrhea and chlamydia most commonly present with dysuria and penile discharge, neither of which is present in this patient. Although it may be appropriate to perform testing for other sexually transmitted infections, gonorrhea would be an unlikely explanation for this patient's painful genital ulcer.

(Choice E) Granuloma inguinale is characterized by painless, extensive ulcerative lesions, typically without lymphadenopathy.

(Choice F) Molluscum contagiosum is a contagious disease caused by infection with a DNA poxvirus. Lesions are smooth, whitish or skin-colored, firm, somewhat pearly papules that measure about 2-6 mm and often have a central umbilication.

(Choice G) Primary syphilis commonly presents as a characteristically painless single genital ulcer called a chancre. The diagnosis is established by identification of the organisms on darkfield microscopy, serologic testing, or syphilis antibody testing. Secondary syphilis is often characterized by systemic symptoms, lymphadenopathy, grey mucous patches, raised grey genital papules (condylomata lata), and a diffuse rash involving the palms and soles.

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in men and the vulvovaginal and cervical areas in women.

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(Choice G) Primary syphilis commonly presents as a characteristically painless single genital ulcer called a chancre. The diagnosis is established by identification of the organisms on darkfield microscopy, serologic testing, or syphilis antibody testing. Secondary syphilis is often characterized by systemic symptoms, lymphadenopathy, grey mucous patches, raised grey genital papules (condylomata lata), and a diffuse rash involving the palms and soles.

(Choice H) Penile squamous cell cancer can present as lumps or ulcers, sometimes with adenopathy. However, the lesions are typically painless, and average age at presentation is 50.

Educational objective:

Chancroid, due to *Haemophilus ducreyi*, presents as deep, painful (you "do cry" with *H ducreyi*) ulcers with ragged borders that are associated with a grey exudate and inguinal lymphadenopathy. Diagnosis is established by Gram stain and culture of the organism from a scraping of the ulcer base.

References

- Diagnosis and management of genital ulcers.
- Chancroid: clinical manifestations, diagnosis and management

Microbiology	Infectious Diseases	Chancroid
Subject	System	Topic

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www.ncbi.nlm.nih.gov/pubmed/25418193

A 76-year-old woman comes to the emergency department due to fever and burning with urination for 2 days and right-sided back pain for 1 day. Her temperature is 38.3 C (101 F), blood pressure is 110/80 mm Hg, pulse is 94/min, and respirations are 18/min. Examination is notable for right-sided flank tenderness to palpation. Urinalysis is positive for nitrites, leukocyte esterase, and bacteria. Urine and blood cultures are obtained, and the patient is started on antibiotic therapy. The next day, urine culture grows >100,000 colony-forming units/mL of *Escherichia coli*. The organism is found to have a methyltransferase that methylates ribosomal RNA. This enzyme most likely confers resistance to which of the following classes of antibiotics?

A. Aminoglycosides
B. Carbapenems
C. Glycopeptides
D. Penicillins
E. Quinolones

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days and right-sided back pain for 1 day. Her temperature is 38.3 C (101 F), blood pressure is 110/80 mm Hg, pulse is 94/min, and respirations are 18/min. Examination is notable for right-sided flank tenderness to palpation. Urinalysis is positive for nitrites, leukocyte esterase, and bacteria. Urine and blood cultures are obtained, and the patient is started on antibiotic therapy. The next day, urine culture grows >100,000 colony-forming units/mL of *Escherichia coli*. The organism is found to have a methyltransferase that methylates ribosomal RNA. This enzyme most likely confers resistance to which of the following classes of antibiotics?

- A. Aminoglycosides (82%)
- B. Carbapenems (3%)
- C. Glycopeptides (3%)
- D. Penicillins (4%)
- E. Quinolones (7%)

Correct

82%

39 secs

10/04/2020

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Common antibiotic resistance mechanisms	
Penicillins	• Beta-lactamase, ESBL • Mutated PBP • Mutated porin protein
Vancomycin	• Mutated peptidoglycan cell wall • Impaired influx/increased efflux
Quinolones	• Mutated DNA gyrase • Impaired influx/increased efflux
Aminoglycosides	• Aminoglycoside-modifying enzymes • Mutated ribosomal subunit protein • Mutated porin protein
Tetracyclines	• Impaired influx/increased efflux • Inactivated enzyme
Rifamycins	• Mutated RNA polymerase

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Aminoglycosides interfere with the aminoacyl binding site on the 30S **ribosomal** subunit. Binding of aminoglycoside causes the cell to misread mRNA and, as a result, it is unable to perform protein synthesis. An important mechanism of **resistance** to aminoglycosides is the **methylation** of the aminoglycoside-binding portion of the ribosome, which inhibits the ability of aminoglycosides to interfere with protein translation. Other common resistance mechanisms are the production of enzymes that inactivate the drug by altering its chemical structure or the production of an efflux pump that decreases the drug's intracellular concentration.

(Choices B and D) Carbapenems and penicillins function similarly to other beta-lactam antibiotics by inhibiting a family of enzymes responsible for cell wall construction. Resistance to both can occur through alteration of the antibiotic binding site on the enzyme; decreased permeability of the antibiotic into the cell wall; or production of beta-lactamases, which alter the antibiotic structure by cleaving protein bonds in the antibiotic and inactivating it.

(Choice C) Vancomycin is a glycopeptide antibiotic used to treat methicillin-resistant *Staphylococcus aureus* infections. It binds to D-alanine-D-alanine, thereby preventing peptidoglycan cell wall synthesis. Bacteria have been identified in which a D-alanine is replaced by a D-lactate, leading to vancomycin resistance.

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wall; or production of beta-lactamases, which alter the antibiotic structure by cleaving protein bonds in the antibiotic and inactivating it.

(Choice C) Vancomycin is a glycopeptide antibiotic used to treat methicillin-resistant *Staphylococcus aureus* infections. It binds to D-alanine-D-alanine, thereby preventing peptidoglycan cell wall synthesis. Bacteria have been identified in which a D-alanine is replaced by a D-lactate, leading to vancomycin resistance.

(Choice E) Resistance to the quinolones occurs by alteration of the genes encoding for DNA gyrase and topoisomerase IV, development of an efflux pump, or alteration of the membrane diffusion channels used by the antibiotic.

Educational objective:
Aminoglycosides work by interfering with the 30S ribosomal subunit and causing the cell to misread messenger RNA, thereby halting protein synthesis. An important mechanism of resistance is the methylation of the aminoglycoside-binding portion of the ribosome, which inhibits the ability of aminoglycoside to interfere with protein translation.

References

- Versatility of aminoglycosides and prospects for their future.

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A 52-year-old man is brought to the emergency department due to worsening right leg pain, fever, and confusion. The patient injured his leg while operating a motorized watercraft on the ocean near Florida 2 days ago. Temperature is 38.9 C (102 F), blood pressure is 90/50 mm Hg, and pulse is 120/min. The patient is lethargic and diaphoretic. Physical examination reveals a small laceration on the dorsum of the right foot with surrounding edema, erythema, and several hemorrhagic bullae. Leukocyte count and serum lactic acid levels are elevated. Intravenous fluids and empiric antibiotics are administered, and surgical debridement of the wound is performed. Blood and wound cultures yield curved gram-negative rods. Which of the following is the greatest risk factor for this patient's infection?

A. Bacterial nasal colonization
B. Condition causing iron overload
C. Exposure to infected rodent urine
D. Lack of booster immunization
E. Recent broad-spectrum antibiotic use

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confusion. The patient injured his leg while operating a motorized watercraft on the ocean near Florida 2 days ago. Temperature is 38.9 C (102 F), blood pressure is 90/50 mm Hg, and pulse is 120/min. The patient is lethargic and diaphoretic. Physical examination reveals a small laceration on the dorsum of the right foot with surrounding edema, erythema, and several hemorrhagic bullae. Leukocyte count and serum lactic acid levels are elevated. Intravenous fluids and empiric antibiotics are administered, and surgical debridement of the wound is performed. Blood and wound cultures yield curved gram-negative rods.

Which of the following is the greatest risk factor for this patient's infection?

A. Bacterial nasal colonization (6%)
B. Condition causing iron overload (23%)
C. Exposure to infected rodent urine (30%)
D. Lack of booster immunization (24%)
E. Recent broad-spectrum antibiotic use (14%)

Correct

23%

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Vibrio vulnificus	
Epidemiology	• Curved, gram-negative, free-living in **salt water** • High concentrations in warm months • Ingestion (**raw oysters**) or wound infection • ↑ Risk in those with **liver disease** & **iron overload***
Manifestations	• Rapidly progressive (often <12 hours) • **Septicemia** – Septic shock, bullous lesions • **Cellulitis** – Hemorrhagic bullae, necrotizing fasciitis

*Hereditary hemochromatosis is particularly high risk as iron acts as a growth catalyst.

Vibrio vulnificus is a curved, gram-negative, free-living bacterium that grows in brackish coastal water and **marine** environments. This bacterium is found in greatest concentrations in the summer months, comprising as much as 8% of the total bacteria in some areas. *V vulnificus* infections are primarily acquired through the consumption of **raw oysters** (which concentrate the bacterium) or **wound contamination** during recreational water activities or the handling of raw seafood. Most patients who become ill have **liver disease** (eg, alcoholic cirrhosis, viral hepatitis); those with **iron overload** (eg,

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acquired through the consumption of **raw oysters** (which concentrate the bacterium) or **wound contamination** during recreational water activities or the handling of raw seafood. Most patients who become ill have **liver disease** (eg, alcoholic cirrhosis, viral hepatitis); those with **iron overload** (eg, hemochromatosis) are at particularly high risk as free iron acts as an exponential growth catalyst for the bacterium.

Healthy patients with *V vulnificus* wound contamination usually develop a mild cellulitis, but those with iron overload or liver disease are at high risk for **rapidly progressive necrotizing fasciitis** with hemorrhagic, bullous lesions and septic shock (eg, hypotension, elevated lactic acid level). In these patients, urgent antibiotics, surgery, and blood pressure support are usually required to prevent death.

(Choice A) *Staphylococcus aureus* colonizes the nasopharynx and is a leading cause of skin/soft-tissue abscess. However, *S aureus* is a catalase-positive, gram-positive bacterium.

(Choice C) *Leptospira* species are highly motile, gram-negative spirochetes that are often transmitted via contaminated rat urine. Leptospirosis is often mild or asymptomatic but may cause fever, myalgia, headache, multiorgan failure, or death. This patient who developed symptoms after a sustaining a wound while boating is more likely to have a *V vulnificus* infection.

(Choice D) *Clostridium tetani* is an anaerobic, gram-positive, spore-forming rod-shaped bacterium that can

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(Choice C) *Leptospira* species are highly motile, gram-negative spirochetes that are often transmitted via contaminated rat urine. Leptospirosis is often mild or asymptomatic but may cause fever, myalgia, headache, multiorgan failure, or death. This patient who developed symptoms after a sustaining a wound while boating is more likely to have a *V vulnificus* infection.

(Choice D) *Clostridium tetani* is an anaerobic, gram-positive, spore-forming rod-shaped bacterium that can inoculate wounds contaminated with soil. It elaborates an exotoxin (tetanus toxin) that disinhibits anterior horn cells and results in painful muscle contractions, lock-jaw, and difficulty swallowing.

(Choice E) *Clostridium difficile* is most common in individuals who have recently taken broad-spectrum antibiotics, which disrupts gastrointestinal flora and allows the organism to proliferate. Patients usually develop diarrhea, fever, and abdominal pain.

Educational objective:
Vibrio vulnificus is a curved, gram-negative, free-living bacterium that grows in marine environments. Transmission primarily occurs due to the consumption of raw seafood (eg, oysters) or wound contamination. Manifestations are often mild, but individuals with liver disease or iron overload are at very high risk of severe, fulminant infection (eg, sepsis, necrotizing fascitis).

Microbiology Infectious Diseases Vibrio vulnificus

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A 5-week-old girl is brought to the emergency department due to several hours of fever, irritability, and vomiting. This morning she was warm to the touch and refused to drink. Her temperature is 40.1 C (104.2 F). Lumbar puncture reveals cerebrospinal fluid pleocytosis; additional fluid is sent for Gram stain and culture. Empiric cefotaxime and vancomycin therapy is initiated. However, no clinical improvement is seen. Cerebrospinal fluid culture yields an organism that is resistant to cefotaxime. Which of the following organisms is most likely causing this patient's infection?

A. *Haemophilus influenzae*
B. *Listeria monocytogenes*
C. *Neisseria meningitidis*
D. *Streptococcus agalactiae*
E. *Streptococcus pneumoniae*

Submit

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A 5-week-old girl is brought to the emergency department due to several hours of fever, irritability, and vomiting. This morning she was warm to the touch and refused to drink. Her temperature is 40.1 C (104.2 F). Lumbar puncture reveals cerebrospinal fluid pleocytosis; additional fluid is sent for Gram stain and culture. Empiric cefotaxime and vancomycin therapy is initiated. However, no clinical improvement is seen. Cerebrospinal fluid culture yields an organism that is resistant to cefotaxime. Which of the following organisms is most likely causing this patient's infection?

A. ~~*Haemophilus influenzae*~~ (12%)

✓ B. *Listeria monocytogenes* (55%)

C. ~~*Neisseria meningitidis*~~ (8%)

D. *Streptococcus agalactiae* (18%)

E. ~~*Streptococcus pneumoniae*~~ (4%)

Correct

55% Answered correctly

01 min, 23 secs Time Spent

10/11/2020 Last Updated

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Cephalosporin-resistant organisms	
Organism	**Reason**
Listeria monocytogenes	Resistant penicillin-binding proteins
Methicillin-resistant *Staphylococcus*	
Enterococci	
Atypicals (eg *Mycoplasma*, *Chlamydia*)	No cell wall

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This infant with high fever, irritability, vomiting, and cerebrospinal fluid pleocytosis has **meningitis**. Empiric treatment with cefotaxime and vancomycin would cover the majority of likely pathogens in this age group including *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*, group B streptococcus, and *Escherichia coli*. However, it would not cover ***Listeria monocytogenes***, which has **intrinsic resistance** to third-generation **cephalosporins** (eg, cefotaxime, ceftriaxone) due to the presence of **penicillin-binding proteins** that have a **low-affinity** for this drug class. Coverage of *Listeria* requires the addition of **ampicillin**, a beta-lactam antibiotic with a specialized side-group that allows it to bind to and

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intrinsic resistance to third-generation **cephalosporins** (eg, cefotaxime, ceftriaxone) due to the presence of **penicillin-binding proteins** that have a **low-affinity** for this drug class. Coverage of *Listeria* requires the addition of **ampicillin**, a beta-lactam antibiotic with a specialized side-group that allows it to bind to and inactivate the penicillin binding proteins of *Listeria*.

(Choice A) Although many *Haemophilus influenzae* organisms produce beta lactamases, they are effectively treated with a beta lactam/beta lactamase inhibitor (eg, amoxicillin/clavulanate) or with third-generation cephalosporins.

(Choice C) *Neisseria meningitidis* is effectively treated with third-generation cephalosporins.

(Choice D) *Streptococcus agalactiae* (group B *Streptococcus*) is universally susceptible to ampicillin or penicillin as well as third-generation cephalosporins.

(Choice E) *Streptococcus pneumoniae* is the most common cause of meningitis in older infants and children. Although this organism has increasing penicillin and cephalosporin resistance, vancomycin provides effective coverage (and would result in symptomatic improvement).

Educational objective:
Ampicillin is the treatment of choice for *Listeria*, which is not sensitive to cephalosporins. *Listeria* most commonly causes disease in those with deficient cell-mediated immunity, such as young infants or

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(Choice A) Although many *Haemophilus influenzae* organisms produce beta lactamases, they are effectively treated with a beta lactam/beta lactamase inhibitor (eg, amoxicillin/clavulanate) or with third-generation cephalosporins.

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Educational objective:

Ampicillin is the treatment of choice for *Listeria*, which is not sensitive to cephalosporins. *Listeria* most commonly causes disease in those with deficient cell-mediated immunity, such as young infants or immunocompromised patients.

References

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC172923/pdf/100345.pdf

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A group of researchers collected demographic and clinical data from multiple hospitals across the nation to determine epidemiological features of nosocomial bloodstream infections. In this study, a nosocomial bloodstream infection was diagnosed if blood cultures drawn 48 hours after admission yielded a pathogenic organism. Analysis of the data collected over several decades shows that staphylococci are increasingly responsible for the identified cases. An increased use of which of the following is most likely the underlying cause of the observed trend?

A. Bioprosthetic heart valves
B. Broad-spectrum antibiotics
C. Illicit injection drugs
D. Immunomodulating therapies
E. Indwelling urinary catheters
F. Intravascular catheters

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A group of researchers collected demographic and clinical data from multiple hospitals across the nation to determine epidemiological features of nosocomial bloodstream infections. In this study, a nosocomial bloodstream infection was diagnosed if blood cultures drawn 48 hours after admission yielded a pathogenic organism. Analysis of the data collected over several decades shows that staphylococci are increasingly responsible for the identified cases. An increased use of which of the following is most likely the underlying cause of the observed trend?

A. Bioprosthetic heart valves (6%)
B. Broad-spectrum antibiotics (29%)
C. Illicit injection drugs (9%)
D. Immunomodulating therapies (0%)
E. Indwelling urinary catheters (10%)
F. Intravascular catheters (42%)

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Most common pathogens causing nosocomial bloodstream infections
• Coagulase-negative staphylococci • *Staphylococcus aureus* • Enterococci • *Candida* species

Approximately 250,000 **nosocomial bloodstream infections** (BSIs) are estimated to occur in the United States each year. Prior to the 1980s, the leading cause was gram-negative aerobic organisms such as *Escherichia coli* that spread from primary infections in the genitourinary or gastrointestinal tract. However, the increasing use of **intravascular catheters**, which provide a portal of entry for **skin flora** to reach the bloodstream, has led to a shift in the underlying microbiology of BSI; most cases are now caused by skin commensals such as **coagulase-negative staphylococci** and ***Staphylococcus aureus***.

BSI is most common in those who have **long-term** (>12 days) central venous access as this provides sufficient time for skin flora to colonize the internal/external lumen of the catheter, to replicate within a biofilm of host (fibrin) and bacterial (glycoprotein) components, and to subsequently spread to the

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bloodstream. BSI should be suspected when a patient with an intravascular catheter develops new-onset fever or bacteremia.

(Choice A) Although *S aureus* is a leading cause of infective endocarditis in patients with artificial heart valves, bacteremia is much more commonly caused by intravascular devices.

(Choice B) The increased use of broad-spectrum antibiotics is associated with the development of drug-resistant organisms, including methicillin-resistant *S aureus* (MRSA). Although MRSA is a common cause of skin abscess and necrotizing pneumonia, the majority of *S aureus* bacteremia is caused by intravascular catheters.

(Choice C) Injection drug use is a major risk factor for *S aureus* abscess, bacteremia, and infective endocarditis. However, injection drug use causes far fewer BSIs than intravenous catheters.

(Choice D) Immunosuppression increases the risk of BSI due to reduced immunosurveillance. However, BSI is far more often due to the use of intravascular catheters.

(Choice E) Indwelling urinary catheters increase the risk of urinary infection with subsequent hematogenous spread of the organism. However, most cases are caused by gram-negative enteric organisms such as *E coli*.

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(Choice C) Injection drug use is a major risk factor for *S aureus* abscess, bacteremia, and infective endocarditis. However, injection drug use causes far fewer BSIs than intravenous catheters.

(Choice D) Immunosuppression increases the risk of BSI due to reduced immunosurveillance. However, BSI is far more often due to the use of intravascular catheters.

(Choice E) Indwelling urinary catheters increase the risk of urinary infection with subsequent hematogenous spread of the organism. However, most cases are caused by gram-negative enteric organisms such as *E coli*.

Educational objective:
Nosocomial bloodstream infections are usually associated with intravascular catheters, which allow skin commensals such as *Staphylococcus aureus* and coagulase-negative staphylococci to enter the bloodstream.

Microbiology	Infectious Diseases	Catheter related bloodstream infection
Subject	System	Topic

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A 13-year-old boy is brought to the clinic by his parents due to a change in behavior. His special education teacher reported that for the last several weeks he has frequently taken off his shoes to scratch his feet during class. The patient has a history of learning disability but is otherwise healthy. Examination shows erythema and excoriations between the toes of both feet. Microscopy of skin scrapings from the rash is shown in the exhibit. Which of the following antimicrobial drugs is likely to be the most effective against the pathogen causing this patient's condition?

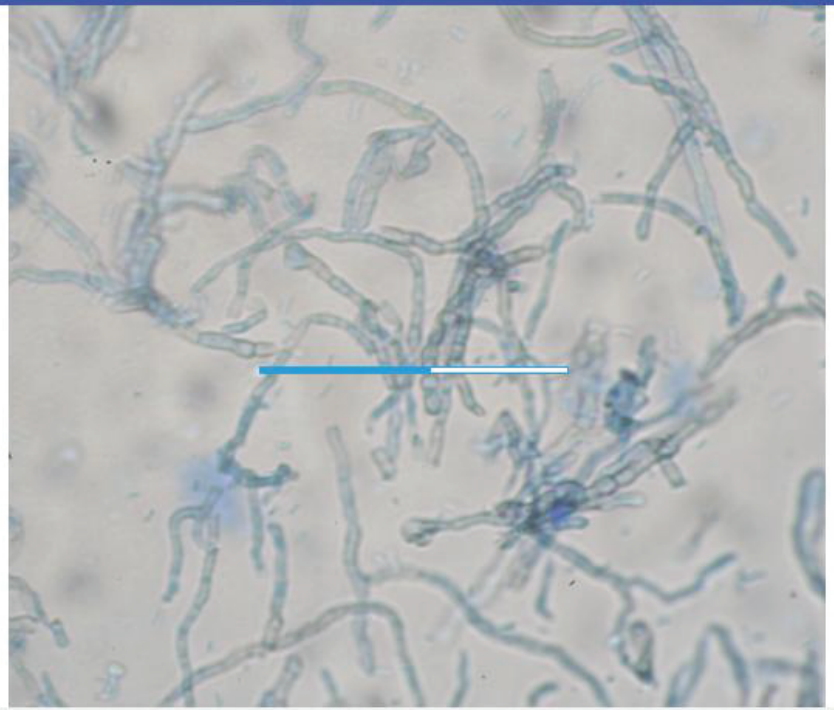
A. Albendazole
B. Clotrimazole
C. Mupirocin
D. Nystatin
E. Permethrin

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A 6-hour-old boy is evaluated in the newborn nursery due to temperature instability, grunting, and lethargy. The patient was born at full term to a 21-year-old woman who came to the emergency department in active labor with ruptured membranes; she had not received adequate prenatal care. On physical examination, the boy is hypothermic, tachycardic, and tachypneic, and he has mottled skin. Blood samples are obtained, and empiric antibiotics are initiated for the treatment of sepsis. Cultures on blood agar grow bacterial colonies with a narrow zone of clear hemolysis. When these bacteria are grown in the presence of *Staphylococcus aureus*, the zone of hemolysis is enhanced around the staphylococcal colonies. Which of the following is the most likely pathogen infecting this patient?

A. *Escherichia coli*
B. *Enterococcus faecalis*
C. *Staphylococcus epidermidis*
D. *Streptococcus agalactiae*
E. *Streptococcus pneumoniae*

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The patient was born at full term to a 21-year-old woman who came to the emergency department in active labor with ruptured membranes; she had not received adequate prenatal care. On physical examination, the boy is hypothermic, tachycardic, and tachypneic, and he has mottled skin. Blood samples are obtained, and empiric antibiotics are initiated for the treatment of sepsis. Cultures on blood agar grow bacterial colonies with a narrow zone of clear hemolysis. When these bacteria are grown in the presence of *Staphylococcus aureus*, the zone of hemolysis is enhanced around the staphylococcal colonies. Which of the following is the most likely pathogen infecting this patient?

A. ~~*Escherichia coli*~~ (3%)

B. ~~*Enterococcus faecalis*~~ (3%)

C. ~~*Staphylococcus epidermidis*~~ (1%)

D. *Streptococcus agalactiae* (85%)

E. *Streptococcus pneumoniae* (5%)

Correct

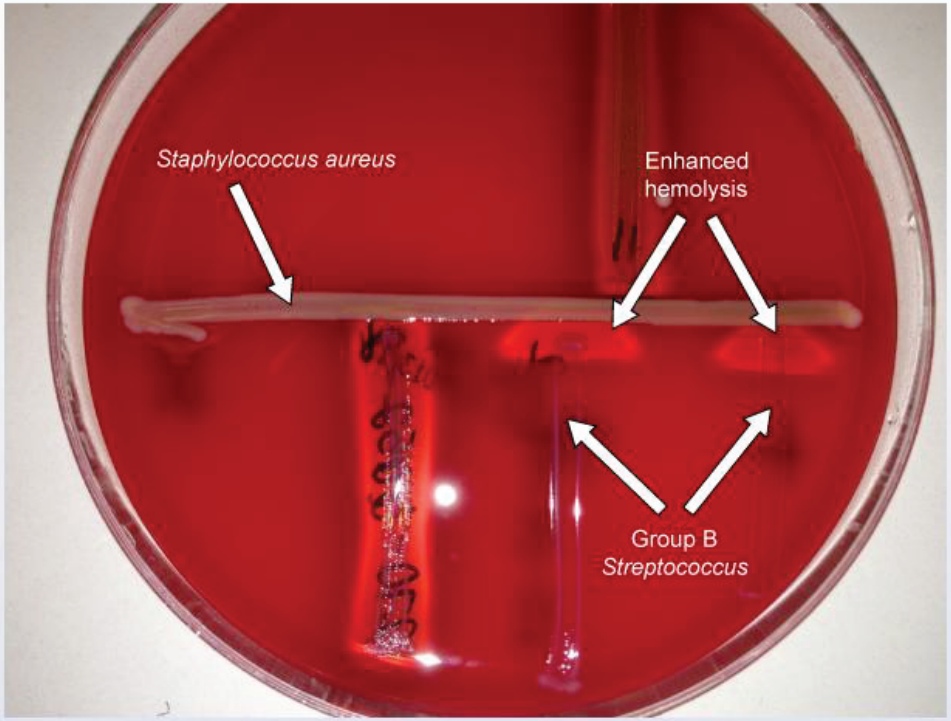
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Streptococcus agalactiae (group B *Streptococcus* [GBS]) is often a normal commensal of the genitourinary and gastrointestinal tracts of pregnant women. Those who are colonized and do not receive

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Streptococcus agalactiae (group B *Streptococcus* [GBS]) is often a normal commensal of the genitourinary and gastrointestinal tracts of pregnant women. Those who are colonized and do not receive intrapartum antibiotic prophylaxis can transmit the bacteria to the fetus during passage through the vaginal canal, leading to neonatal sepsis (eg, irritability, lethargy, grunting, tachypnea, temperature instability, hypotension) within hours of birth.

GBS is a leading cause of **early neonatal sepsis** and can be identified by the following laboratory features:

- **Narrow zone of beta-hemolysis** (clear) when plated on blood agar.
- **Production of CAMP factor**, a phospholipase that enhances the activity of beta-hemolysins secreted by certain strains of *Staphylococcus aureus*. Testing for CAMP factor **(CAMP test)** can confirm the presence of GBS; this test plates suspected GBS colonies perpendicular to an appropriate *S aureus* strain and evaluates for enhanced areas of hemolysis (arrow-shaped zones in the image above).

GBS is also catalase-negative (as are all streptococci), contains the Lancefield group B antigen in its cell wall, and hydrolyzes hippurate.

(Choice A) *Escherichia coli*, a gram-negative rod, is a common cause of early neonatal sepsis. Although *E coli* generates beta-hemolysins, it does not produce CAMP factor; therefore, enhancement of *S aureus*

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E coli generates beta-hemolysins, it does not produce CAMP factor; therefore, enhancement of *S aureus* hemolysis does not occur.

(Choice B) *Enterococcus faecalis*, a gram-positive cocci, is a common cause of sepsis in preterm neonates but is rare in those born at term. In addition, it does not hemolyze red blood cells (gamma hemolytic) or generate camp factor.

(Choice C) *Staphylococcus epidermidis*, a gram-positive coccus that grows in clusters, is a common skin commensal that does not cause hemolysis when plated on blood agar.

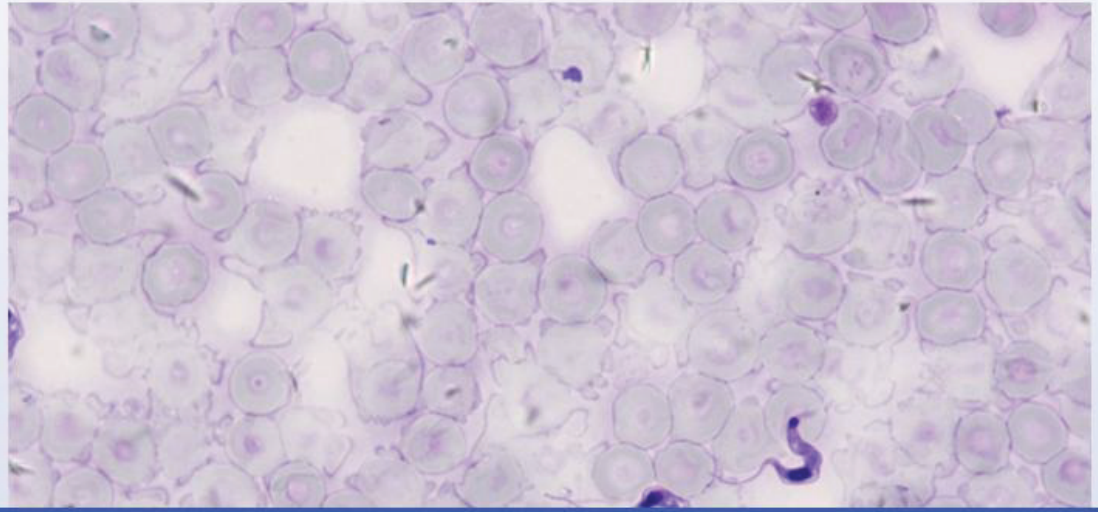
(Choice E) *Streptococcus pneumoniae*, a lancet-shaped, gram-positive bacterium, is alpha-hemolytic (partial, green hemolysis) in aerobic conditions and beta-hemolytic in anaerobic conditions. It does not generate CAMP factor.

Educational objective:
Streptococcus agalactiae (group B *Streptococcus*), one of the most common causes of early neonatal sepsis, is typically identified by the presence of a narrow zone of beta-hemolysis when plated on blood agar. It is also identified by the production of CAMP factor, which enhances beta-hemolysis by particular strains of *Staphylococcus aureus*.

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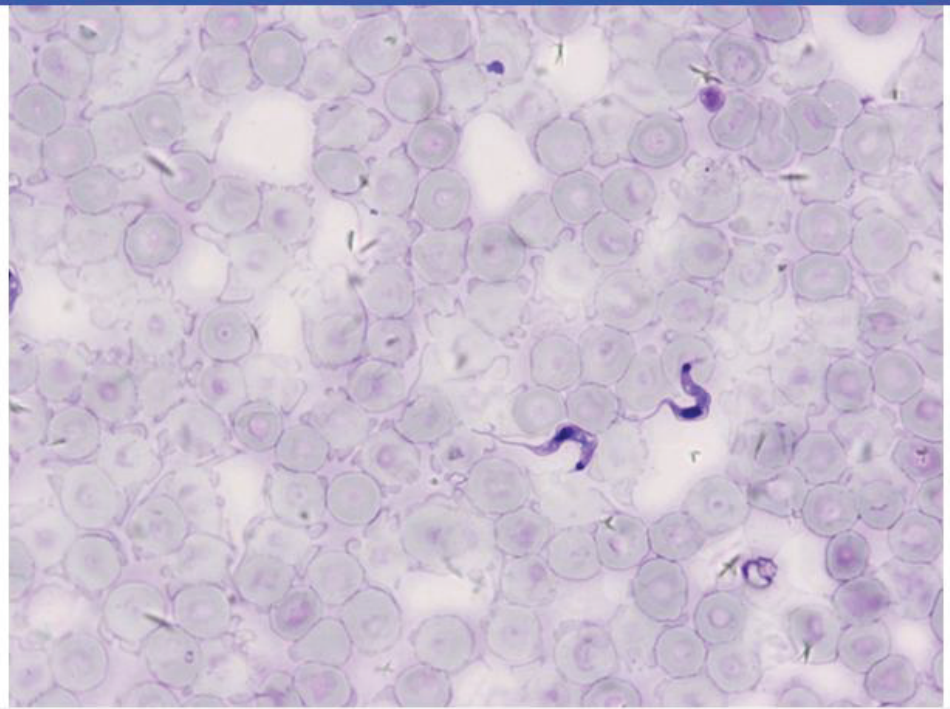
A 26-year-old previously healthy man comes to the emergency department due to fever, malaise, anorexia, and painless swelling of the left eye. His symptoms began after a month-long anthropology trip to rural Bolivia. During his stay, he lived in an adobe house with a thatched roof and unnetted windows and doors. Temperature is 38.3 C (101 F). Physical examination shows left-sided periorbital swelling and conjunctival erythema with no discharge. The remainder of the physical examination, including right eye examination, shows no abnormalities. Giemsa-stained peripheral blood smear is shown below:



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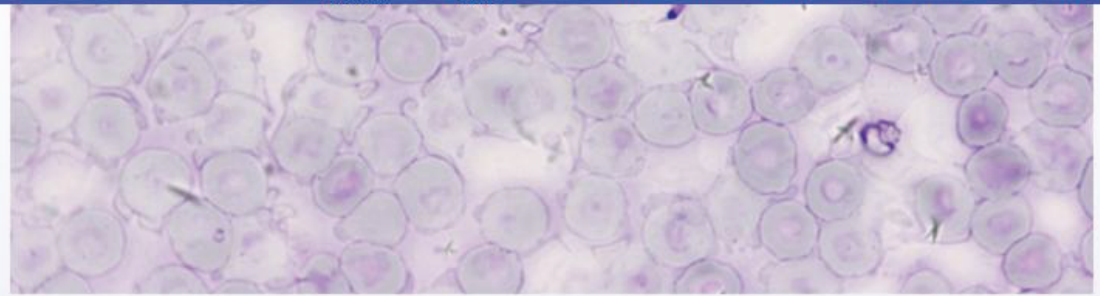
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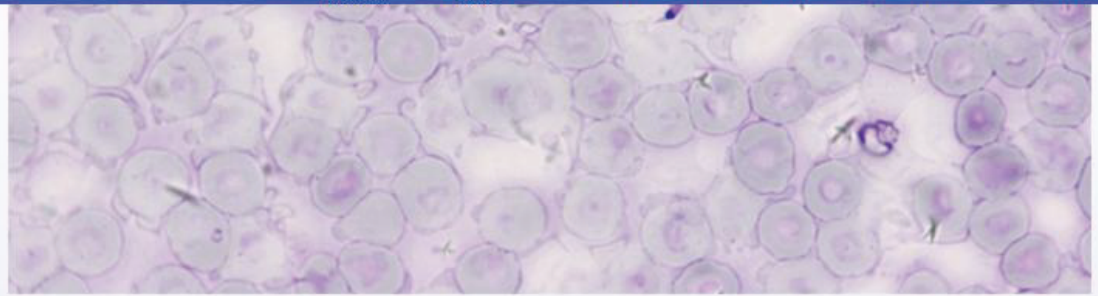


This patient is at greatest risk for which of the following complications if his condition is left untreated?

A. Ascending aortic aneurysm
B. Calcified brain lesions
C. Cardiac arrhythmias
D. Large joint arthritis
E. Periportal liver fibrosis

Submit

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This patient is at greatest risk for which of the following complications if his condition is left untreated?

A. Ascending aortic aneurysm (4%)
B. Calcified brain lesions (10%)
C. Cardiac arrhythmias (57%)
D. Large joint arthritis (7%)
E. Periportal liver fibrosis (19%)

Correct
57%
23 secs
11/17/2020

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Chagas disease is a vector-borne protozoan illness endemic to most Latin American countries. Risk is greatest in those with long-term domestic exposure to the **Triatomine bug**, which nests in thatched roofing and the cracks of adobe or unfinished brick. Transmission occurs when the bug feeds on human blood during the night and defecates the underlying pathogen, ***Trypanosoma cruzi***, into the bite wound.

Chagas disease is divided into 2 phases:

- The acute phase (8-12 weeks after transmission) is characterized by circulating trypomastigotes that are detectable on blood microscopy. Most patients are asymptomatic, but a minority develop nonspecific symptoms (eg, fever, malaise, anorexia) and inflammation/swelling at the site of inoculation (eg, eye swelling following conjunctival inoculation).
- The chronic phase begins when the immune system eliminates circulating parasitemia, leading to resolution of acute symptoms. Patients subsequently develop a prolonged asymptomatic phase ("indeterminate form"), whereby serology is positive for *T cruzi*, but there are no symptoms, signs, detectable parasitemia, or indications of end-organ damage. After 1-3 decades, a minority of those with asymptomatic chronic infection develop end-organ disease of the heart or gastrointestinal system.

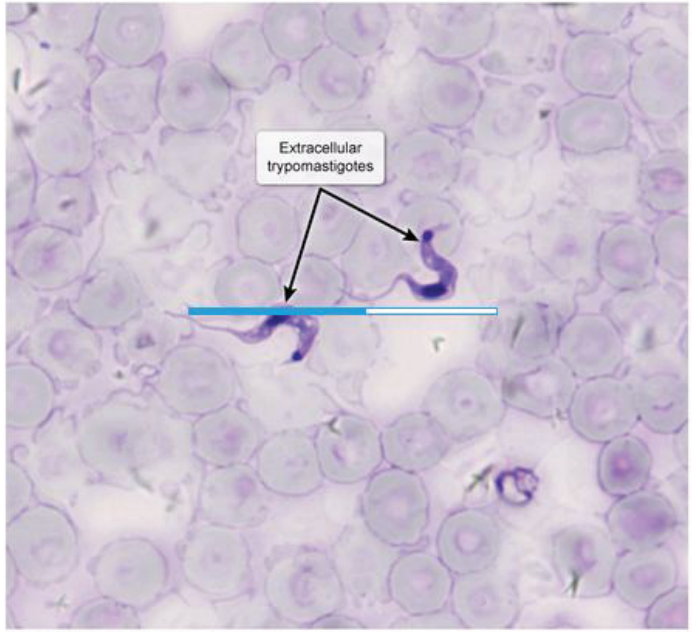
Chronic Chagas cardiomyopathy is the most common complication of Chagas disease. It is thought to be caused by chronic, low-grade, parasite-mediated myocarditis, which leads to the progressive destruction

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Trypanosoma cruzi



Peripheral blood smear – Giemsa stain

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be caused by chronic, low-grade, parasite-mediated myocarditis, which leads to the progressive destruction

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with asymptomatic chronic infection develop end-organ disease of the heart or gastrointestinal system.

Chronic Chagas cardiomyopathy is the most common complication of Chagas disease. It is thought to be caused by chronic, low-grade, parasite-mediated myocarditis, which leads to the progressive destruction of cardiac fibers and subsequent cardiac fibrosis. Common complications include biventricular heart failure, cardiac **arrhythmias** (particularly ventricular arrhythmias), and **ventricular aneurysm** with intracardiac thrombus (leads to thromboembolic disease/stroke).

(Choice A) *Treponema pallidum* has an affinity for the aortic wall and can cause ascending aortic aneurysms (syphilitic aortitis) in patients with tertiary syphilis. Diagnosis is made with serology; treponemes are not visible on standard microscopy.

(Choice B) Neurocysticercosis, which is caused by the larval stage of the pork tapeworm *Taneia solium*, is characterized by the formation of multiple calcified brain lesions that may result in seizures and/or focal neurologic signs several years after transmission. Diagnosis is made with imaging and serology, not blood microscopy.

(Choice D) Lyme disease is a tick-borne illness caused by *Borrelia burgdorferi*. Early localized disease is characterized by a migrating erythematous, bull's-eye rash (erythema migrans) and nonspecific symptoms. Months or years later, patients can develop late manifestations, such as large joint arthritis or Lyme

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(Choice D) Lyme disease is a tick-borne illness caused by *Borrelia burgdorferi*. Early localized disease is characterized by a migrating erythematous, bull's-eye rash (erythema migrans) and nonspecific symptoms. Months or years later, patients can develop late manifestations, such as large joint arthritis or Lyme encephalopathy. *B burgdorferi* is a spirochete and cannot be seen on standard blood microscopy.

(Choice E) Schistosomiasis is transmitted to humans who swim or bathe in fresh water contaminated with cercariae from infected snails. The fluke matures in the liver and spreads to the mesenteric vessels, where it releases eggs that can cause end-organ inflammation and fibrosis (eg, periportal liver fibrosis). Diagnosis is made by identifying eggs in urine or stool, not on blood microscopy.

Educational objective:

Chagas disease is a protozoal illness that is endemic to Latin America. Patients in rural areas are at greatest risk when their houses harbor the vector (Triatome bug) in adobe walls or thatched roofs. Acute infections are often asymptomatic, but patients can develop Chagas cardiomyopathy (eg, heart failure, ventricular arrhythmias, ventricular aneurysms) several decades later.

Microbiology	Infectious Diseases	Chagas disease
Subject	System	Topic

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During the course of a week at an overnight summer camp, 4 children age 7-9 are sent to the camp health center. They each have fever, cough, congestion, sore throat, and red eyes. Physical examination of the children shows bilateral conjunctival injection and an erythematous oropharynx. Auscultation of one child also reveals crackles in the left lower lung field. All the children's symptoms improve over 7 days with supportive care. Which of the following is the most likely cause of the outbreak?

A. Adenovirus
B. Coxsackievirus
C. Influenza virus
D. Norovirus
E. Parvovirus
F. Respiratory syncytial virus

Submit

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During the course of a week at an overnight summer camp, 4 children age 7-9 are sent to the camp health center. They each have fever, cough, congestion, sore throat, and red eyes. Physical examination of the children shows bilateral conjunctival injection and an erythematous oropharynx. Auscultation of one child also reveals crackles in the left lower lung field. All the children's symptoms improve over 7 days with supportive care. Which of the following is the most likely cause of the outbreak?

- A. Adenovirus (75%)
- B. Coxsackievirus (3%)
- C. Influenza virus (5%)
- D. Norovirus (2%)
- E. Parvovirus (1%)
- F. Respiratory syncytial virus (10%)

Correct

75% Answered correctly

46 secs Time Spent

01/19/2021 Last Updated

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Adenovirus	
Epidemiology	• Double-stranded DNA • Transmission via direct contact, fecal-oral route, respiratory droplets • Occurs year-round
Clinical features	• Pharyngoconjunctival fever • Outbreaks in crowded quarters (eg, day care centers, camp dormitories, military barracks)

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Adenovirus infection is a common, usually **self-limiting**, disease caused by a double-stranded DNA genome that is transmitted via direct contact, fecal-oral route, or respiratory droplets. Adenovirus infection occurs year-round and in **outbreaks** in crowded quarters (eg, day care centers, camp dormitories, military barracks).

Viral replication in epithelial cells can give rise to varying manifestations of disease based on serotype, with upper respiratory involvement as the most common. **Pharyngoconjunctival fever** is characterized by the

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barracks).

Viral replication in epithelial cells can give rise to varying manifestations of disease based on serotype, with upper respiratory involvement as the most common. **Pharyngoconjunctival fever** is characterized by the **acute** onset of **fever, cough, congestion, pharyngitis,** and **conjunctivitis**. Physical examination usually reveals an erythematous oropharynx with bilateral, follicular conjunctival injection and serous discharge. Pneumonia occurs in a small percentage of patients, such as the child with focal crackles.

(Choice B) In young children, hand-foot-and-mouth disease is caused by coxsackievirus. Painful vesicles develop in the oropharynx and on the hands (eg, palms, dorsal fingers) and feet (eg, soles, sides). Coxsackievirus can also cause herpangina, an illness characterized by fever with posterior pharyngeal vesicles and without a rash.

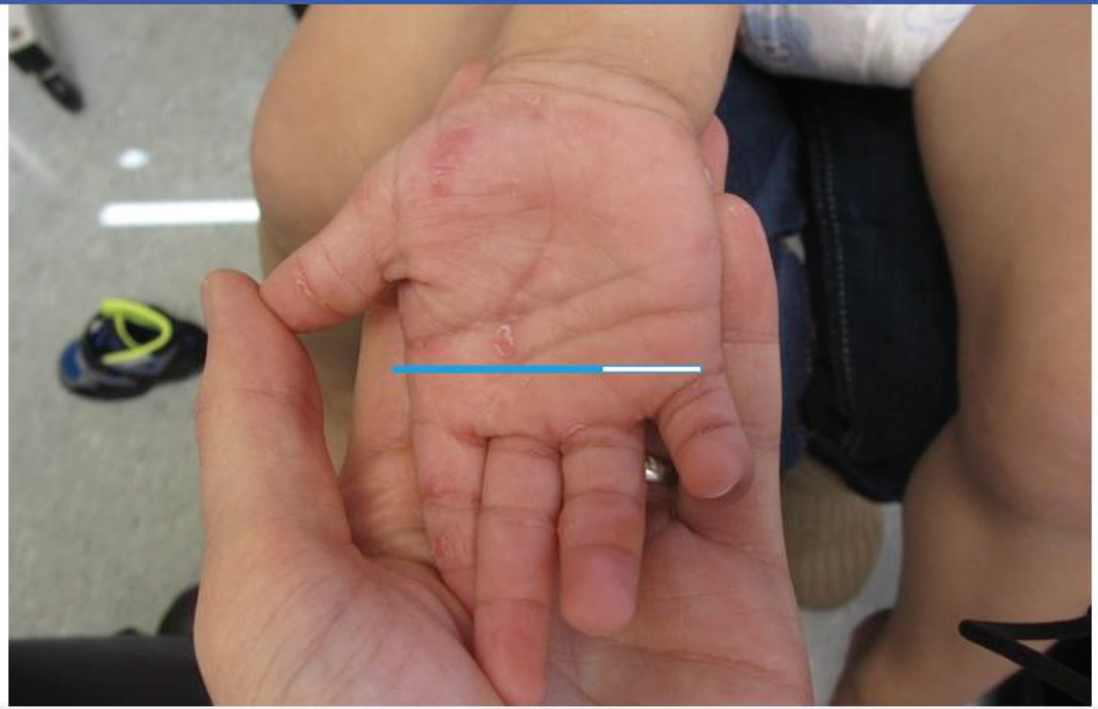
(Choice C) Influenza viruses cause acute onset of high fever, cough, muscle aches, and malaise with a peak incidence during the winter. In children, infection can be complicated by febrile seizures, vomiting, acute otitis media, and pneumonia.

(Choice D) Norovirus causes rapid-onset, self-limiting gastroenteritis in outbreak settings (eg, restaurants, child care facilities, cruise ships). In addition to vomiting and diarrhea, fever, headache, and malaise are common.

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barracks).

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(Choice D) Norovirus causes rapid-onset, self-limiting gastroenteritis in outbreak settings (eg, restaurants, child care facilities, cruise ships). In addition to vomiting and diarrhea, fever, headache, and malaise are common.

(Choice E) Parvovirus B19 causes erythema infectiosum (fifth disease) in school-aged children and presents with fever, malaise, and a classic "slapped cheek" rash.

(Choice F) Respiratory syncytial virus (RSV) classically causes lower respiratory tract disease (eg, bronchiolitis, pneumonia) in infants. Although older children and adults can develop respiratory infection and outbreaks can occur in close quarters, RSV is a seasonal virus that peaks in the winter months.

Educational objective:

Adenovirus is a self-limiting, year-round infection that causes the acute onset of fever, cough, congestion, pharyngitis, and conjunctivitis. This pharyngoconjunctival disease can occur in outbreaks among those living in close quarters (eg, camp dormitories, military barracks).

References

- Adenovirus.

Microbiology	Infectious Diseases	Upper respiratory tract infections
Subject	System	Topic

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(Choice D) Norovirus causes rapid-onset, self-limiting gastroenteritis in outbreak settings (eg, restaurants,

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Subject System Topic

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A 62-year-old man comes to the emergency department due to 3 days of severe sore throat, difficulty swallowing, and hoarseness. He has no chronic medical conditions but has not seen a physician for many years. The patient received recommended childhood vaccinations but has had none since then. He is a farmer and has not traveled recently but has been in contact with migrant farmworkers. Temperature is 38.3 C (101 F), blood pressure is 110/60 mm Hg, and pulse is 116/min. Physical examination reveals pharyngeal erythema and edema with coalescing, gray exudate. Bilateral cervical lymph nodes are enlarged and tender. A rapid streptococcal test result is negative. Throat swab culture grows non-spore–forming, gram-positive rods. Which of the following is most helpful in preventing the systemic complications of this infection in this patient?

A. Airway edema reduction with inhaled epinephrine
B. Antibiotics administration to kill bacteria within the bloodstream
C. Blunting the immune response with glucocorticoids
D. Preformed antibody administration to bind bacterial product
E. Vaccination with inactivated bacterial toxin

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years. The patient received recommended childhood vaccinations but has had none since then. He is a farmer and has not traveled recently but has been in contact with migrant farmworkers. Temperature is 38.3 C (101 F), blood pressure is 110/60 mm Hg, and pulse is 116/min. Physical examination reveals pharyngeal erythema and edema with coalescing, gray exudate. Bilateral cervical lymph nodes are enlarged and tender. A rapid streptococcal test result is negative. Throat swab culture grows non-spore–forming, gram-positive rods. Which of the following is most helpful in preventing the systemic complications of this infection in this patient?

A. Airway edema reduction with inhaled epinephrine (2%)

B. Antibiotics administration to kill bacteria within the bloodstream (19%)

C. Blunting the immune response with glucocorticoids (2%)

✓ D. Preformed antibody administration to bind bacterial product (45%)

✗ E. Vaccination with inactivated bacterial toxin (29%)

Incorrect
Correct answer

45%

01 min, 48 secs

02/03/2021

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Diphtheria	
Epidemiology	• Rare in developed countries due to widespread vaccination • Risk: inadequate vaccination/10-year booster shot
Pathogenesis	• **Toxigenic *Corynebacterium diphtheriae*** colonizes respiratory tract → secretes **diphtheria toxin** → inhibits host protein synthesis (ADP-ribosylation of EF-2) → local and systemic toxin-mediated effects
Manifestations	• Local: **pseudomembranous pharyngitis**, cervical LAD • Systemic: **myocarditis**/heart failure, neurologic toxicity • Pharyngeal edema/pseudomembrane spread can obstruct respiratory tract
Treatment	• **Diphtheria antitoxin** (most important) • Antibiotics

EF-2 = elongation factor-2; **LAD** = lymphadenopathy.

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Diphtheria is caused by infection with toxigenic strains of *Corynebacterium diphtheriae*, a non-spore–forming, gram-positive rod that is transmitted by aerosolized droplets. Cases are rare in the United States due to widespread vaccination efforts. However, infections can occur in those who received inadequate childhood vaccines or those who did not receive booster vaccination every 10 years.

The manifestations of diphtheria are due to the elaboration of **diphtheria toxin** (DT), an exotoxin that **irreversibly inhibits host protein synthesis** by ADP-ribosylation of elongation factor-2. Local effects include pharyngitis and tonsillitis, often with thick, **grey-white pseudomembranes**. Systemic effects are caused by the absorption of DT into the bloodstream and include potentially life-threatening cardiac (eg, myocarditis) and neurologic complications.

The primary treatment for diphtheria is the urgent administration of **diphtheria antitoxin**, which contains **preformed**, **neutralizing antibodies** that binds and inactivates circulating toxin. Because it cannot inhibit the toxin that has already entered cells, it should be administered as soon as possible. Antibiotic therapy (eg, penicillin, erythromycin) is also given to reduce continued elaboration of DT from the nasopharyngeal infection.

(Choice A) Inhaled, racemic epinephrine can be used in the treatment of croup, which usually presents with cough, inspiratory stridor, and/or hoarseness. Epinephrine could reduce airway swelling in patients

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infection.

(Choice A) Inhaled, racemic epinephrine can be used in the treatment of croup, which usually presents with cough, inspiratory stridor, and/or hoarseness. Epinephrine could reduce airway swelling in patients with diphtheria, but it would not inhibit the local and systemic effects of the toxin.

(Choice B) *C diphtheriae* is noninvasive and does not typically enter the bloodstream. Although antibiotics are administered in acute infection, this component of therapy is less important than providing antitoxin to neutralize DT.

(Choice C) Corticosteroids are sometimes used in the treatment of epiglottitis to reduce airway inflammation and limit the risk of airway compromise. Epiglottitis manifestations typically include stridor, drooling, respiratory distress, and the assumption of the "tripod" position. Most cases are caused by infection with *Haemophilus influenzae* type B in unvaccinated individuals.

(Choice E) Active immunization with the diphtheria toxoid (given as part of the childhood DTaP vaccine) prevents diphtheria. Diphtheria toxoid can also be given as part of tetanus boosters in adults. However, the immune response to vaccination is slow; in undervaccinated patients who are acutely ill, administration of preformed antitoxin antibodies is preferred.

Educational objective:

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neutralize DT.

(Choice C) Corticosteroids are sometimes used in the treatment of epiglottitis to reduce airway inflammation and limit the risk of airway compromise. Epiglottitis manifestations typically include stridor, drooling, respiratory distress, and the assumption of the "tripod" position. Most cases are caused by infection with *Haemophilus influenzae* type B in unvaccinated individuals.

(Choice E) Active immunization with the diphtheria toxoid (given as part of the childhood DTaP vaccine) prevents diphtheria. Diphtheria toxoid can also be given as part of tetanus boosters in adults. However, the immune response to vaccination is slow; in undervaccinated patients who are acutely ill, administration of preformed antitoxin antibodies is preferred.

Educational objective:
The primary treatment for diphtheria is diphtheria antitoxin (passive immunization), which inactivates circulating toxin. Antibiotics should also be administered to reduce continued production of toxin.

References

- Diphtheria remains a threat to health in the developing world—an overview.
- Clinical characteristics and management of 676 hospitalized diphtheria cases, Kyrgyz Republic, 1995.

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www.ncbi.nlm.nih.gov/pubmed/10657201

A 52-year-old active smoker comes to the office due to a 2-week history of malaise, shortness of breath, and decreased appetite. The patient has a history of bicuspid aortic valve and hypertension. His temperature is 39 C (102.2 F), blood pressure is 140/80 mm Hg, and pulse is 110/min. On examination, the patient has a systolic ejection murmur at the right upper sternal border that is unchanged from previous visits; there is a new decrescendo diastolic murmur best heard in the third intercostal space at the left sternal border. Laboratory studies show hemoglobin is 9.3 g/dL and leukocytes are 16,500/mm^3. Blood cultures are positive for *Streptococcus gallolyticus* (formerly *S bovis*). Additional workup for this patient should focus on which of the following conditions?

A. Colonic neoplasia
B. Intravenous drug use
C. Lung cancer
D. Oral infection
E. Urinary tract infection

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and decreased appetite. The patient has a history of bicuspid aortic valve and hypertension. His temperature is 39 C (102.2 F), blood pressure is 140/80 mm Hg, and pulse is 110/min. On examination, the patient has a systolic ejection murmur at the right upper sternal border that is unchanged from previous visits; there is a new decrescendo diastolic murmur best heard in the third intercostal space at the left sternal border. Laboratory studies show hemoglobin is 9.3 g/dL and leukocytes are 16,500/mm^3. Blood cultures are positive for *Streptococcus gallolyticus* (formerly *S bovis*). Additional workup for this patient should focus on which of the following conditions?

- A. Colonic neoplasia (83%)
- B. Intravenous drug use (7%)
- C. Lung cancer (1%)
- D. Oral infection (5%)
- E. Urinary tract infection (1%)

Correct

83%

01 min, 03 secs

11/16/2020

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Streptococcus gallolyticus (formerly *S bovis*) is the main human pathogen among nonenterococcal group D streptococci. It causes a **subacute bacterial endocarditis** (SBE) with symptoms similar to those of *S viridans* SBE. *S gallolyticus* is part of the normal flora of the colon, and bacteremia or endocarditis caused by *S gallolyticus* is associated with **colonic cancer** in ~25% of cases. The relationship between *S gallolyticus* and colon cancer is unclear, but every patient with *S gallolyticus* bacteremia with or without endocarditis should be examined for a gastrointestinal tract malignancy.

S gallolyticus endocarditis is also unique in that most cases occur in patients without preexisting valvular abnormality.

(Choice B) Right-sided endocarditis commonly occurs in intravenous drug users and is typically caused by *Staphylococcus aureus*.

(Choices C and E) There is no known association between endocarditis and lung cancer. *S gallolyticus* can cause septic shock, meningitis, or joint infection; it does not typically cause urinary tract infections.

(Choice D) *S viridans* is the most common etiologic agent in subacute bacterial endocarditis following dental work.

Educational objective:

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S gallolyticus endocarditis is also unique in that most cases occur in patients without preexisting valvular abnormality.

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(Choices C and E) There is no known association between endocarditis and lung cancer. *S gallolyticus* can cause septic shock, meningitis, or joint infection; it does not typically cause urinary tract infections.

(Choice D) *S viridans* is the most common etiologic agent in subacute bacterial endocarditis following dental work.

Educational objective:
Streptococcus gallolyticus (formerly *S bovis*) endocarditis and bacteremia are associated with gastrointestinal lesions (colon cancer) in ~25% of cases. When *S gallolyticus* is cultured in the blood, workup for colonic malignancy with colonoscopy is essential.

Microbiology	Infectious Diseases	Endocarditis
Subject	System	Topic

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A 71-year-old man with chronic obstructive pulmonary disease (COPD) is hospitalized due to shortness of breath and wheezing. The patient is treated with bronchodilators and systemic corticosteroids for acute COPD exacerbation. His symptoms improve over the next 2 days. Before being discharged, an intramuscular vaccine containing inactivated viral components, which he normally receives annually, is administered. Several weeks later, the patient comes in close contact with an individual infected with the same virus contained in the vaccine. Which of the following is most likely to occur in this patient as a result of the vaccination?

A. Destruction of infected cells by $CD8^+$ T lymphocytes
B. Impaired intracellular viral assembly
C. Impaired release of viral progeny from cells
D. Inhibition of viral entry into cells
E. Inhibition of viral genome replication

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A 71-year-old man with chronic obstructive pulmonary disease (COPD) is hospitalized due to shortness of breath and wheezing. The patient is treated with bronchodilators and systemic corticosteroids for acute COPD exacerbation. His symptoms improve over the next 2 days. Before being discharged, an intramuscular vaccine containing inactivated viral components, which he normally receives annually, is administered. Several weeks later, the patient comes in close contact with an individual infected with the same virus contained in the vaccine. Which of the following is most likely to occur in this patient as a result of the vaccination?

A. ~~Destruction of infected cells by CD8+ T lymphocytes~~ (46%)

B. ~~Impaired intracellular viral assembly~~ (2%)

✗ C. Impaired release of viral progeny from cells (7%)

✓ D. Inhibition of viral entry into cells (40%)

E. ~~Inhibition of viral genome replication~~ (3%)

Incorrect

40%

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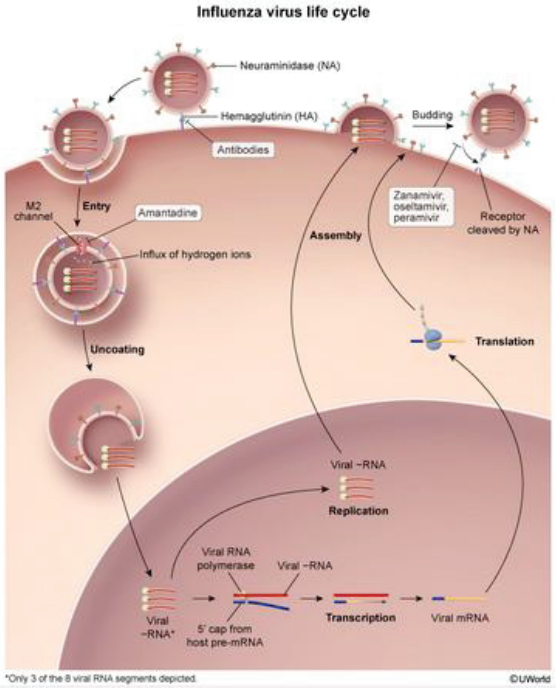
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Influenza vaccination is administered either by injection (inactivated [killed] vaccine) or nasal spray (live attenuated vaccine). Each seasonal influenza vaccine contains antigens (or attenuated virions) from 3 or 4 influenza A and B virus strains. Antigens from multiple influenza types are included in the vaccine because antibodies against 1 strain confer limited or no protection against the others. **Annual vaccination** is recommended due to waning effectiveness over time and because circulating strains of influenza change from year to year. All individuals age >6 months should be immunized, especially health care workers and those at risk of serious complications such as the elderly, patients with chronic illness (eg, chronic obstructive pulmonary disease), and immunocompromised individuals.

Inactivated versions of the influenza vaccine stimulate the formation of **neutralizing antibodies** against the **hemagglutinin antigen** of included strains. Subsequent exposure to a strain of influenza included in the vaccine will not result in infection because the antibodies bind to hemagglutinin, thereby preventing hemagglutinin from attaching to the sialic acid receptor on host respiratory epithelial cells (**preventing viral entry**).

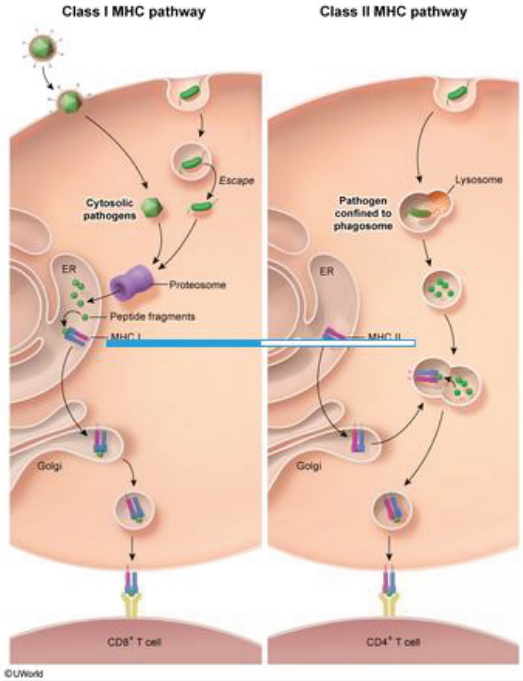
(Choice A) Because inactivated viral vaccines do not infect host cells, they are not processed by the MHC class I pathway and do not stimulate a potent $CD8^+$ T-cell response. In contrast, live attenuated influenza vaccines replicate in nasopharyngeal cells and are displayed on MHC class I molecules, thereby

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(Choice A) Because inactivated viral vaccines do not infect host cells, they are not processed by the MHC class I pathway and do not stimulate a potent $CD8^+$ T-cell response. In contrast, live attenuated influenza vaccines replicate in nasopharyngeal cells and are displayed on MHC class I molecules, thereby generating a strong cytotoxic T-cell response that results in the destruction of the infected cell.

(Choices B and E) Protective antibodies against influenza primarily target the surface glycoproteins and impair viral entry. Immunization does not typically affect viral genomic replication or assembly, which occurs in the interior of the cell and cannot be targeted easily by an antibody response.

(Choice C) Neuraminidase cleaves the terminal sialic acid residues on glycoconjugate receptors, which releases influenza virions from infected cells. Oseltamivir is a sialic acid analogue that competitively inhibits influenza neuraminidase, which prevents release of viral progeny.

Educational objective:
Inactivated (killed or component) viral vaccines primarily generate a humoral immune response against extracellular viral antigens, preventing viral entry into the cell. In contrast, live attenuated viral vaccines can generate a strong cell-mediated immune response that can kill virally-infected cells, in addition to providing humoral immunity.

Immunology Infectious Diseases Immunizations

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A 21-year-old woman comes to the office due to burning on urination and increased urinary frequency for the past 2 days. She has no hematuria, vaginal discharge, or irritation. The patient has no other medical problems. Her temperature is 37 C (98.6 F). Physical examination reveals mild suprapubic tenderness on deep palpation; there is no costovertebral angle tenderness. Urine dipstick is positive for leukocyte esterase and nitrites. The patient is started on trimethoprim, which leads to rapid resolution of her symptoms. Which of the following drugs has the same intracellular target as the drug used to treat this patient?

A. Bacitracin
B. Imipenem
C. Methotrexate
D. Metronidazole
E. Sulfamethoxazole

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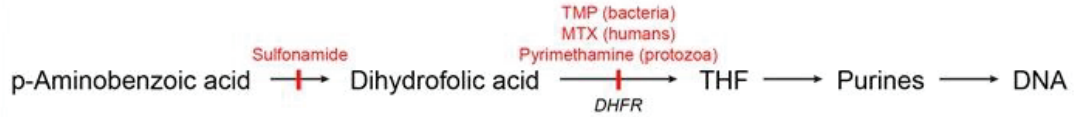
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- A. Bacitracin (4%)
- B. Imipenem (2%)
- ✓ C. Methotrexate (69%)
- D. Metronidazole (2%)
- E. Sulfamethoxazole (20%)

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Trimethoprim-sulfamethoxazole & folic acid pathway



DHFR = dihydrofolate reductase; MTX = methotrexate; THF = tetrahydrofolic acid; TMP = trimethoprim

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Trimethoprim (in bacteria), methotrexate (in human cells), and pyrimethamine (in some protozoa) all prevent the reduction of folic acid to tetrahydrofolate (THF) by inhibiting dihydrofolate reductase (**DHFR**). **Trimethoprim** restricts **bacterial** growth through this process and works particularly well in conjunction with the sulfonamides (eg, sulfamethoxazole), which inhibit an earlier step in the bacterial folic acid pathway (described below). The combination of trimethoprim and sulfamethoxazole produces a "sequential blockade."

Methotrexate is a folate antimetabolite that targets rapidly proliferating **human** cells by halting DNA synthesis through binding DHFR. Methotrexate is cell-cycle specific for the S phase as it prevents synthesis of purine and thymidylic acid (used for pyrimidine synthesis). **Pyrimethamine** is effective for treatment of malaria and toxoplasmosis because it inhibits **parasitic** DHFR.

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(Choice A) Bacitracin prevents mucopeptide transfer into the growing cell wall, thereby inhibiting bacterial cell wall synthesis.

(Choice B) Imipenem binds to penicillin binding proteins, thereby inhibiting the final step of peptidoglycan synthesis in bacterial cell walls. Cilastatin can be used in conjunction with imipenem because it prevents renal metabolism of imipenem by competitively inhibiting dehydropeptidase on the renal tubule brush border.

(Choice D) Metronidazole binds to DNA within susceptible cells, unraveling the helical structure of DNA and breaking its strands. Protein synthesis is inhibited and the cell dies soon thereafter.

(Choice E) As a structural analog of para-aminobenzoic acid (PABA), sulfamethoxazole competes with PABA to inhibit dihydropteroate synthetase, one of the enzymes needed for dihydrofolic acid synthesis. This is an intermediate step in the formation of THF.

Educational objective:
Trimethoprim, methotrexate, and pyrimethamine inhibit dihydrofolate reductase. Trimethoprim restricts bacterial growth through this process, and works particularly well in conjunction with sulfonamide, which inhibits an earlier step in the bacterial folic acid pathway.

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A 24-year-old woman, gravida 1 para 0, at 26 weeks gestation comes to the emergency department due to abdominal cramping and vaginal bleeding. She recently emigrated from Bolivia and reports no prior medical problems. The patient's only medication is a daily multivitamin. Immunization status is unknown. The patient spontaneously delivers a stillborn fetus with multiple congenital malformations. Fetal autopsy reveals microcephaly with thin cerebral cortices, ventriculomegaly, and subcortical calcifications. Viral RNA of a neurotropic virus is detected in body fluids of the mother and the fetus. Transplacental transmission of this virus causes apoptosis of neural progenitor cells in the developing fetus, leading to disruption of neuronal proliferation, migration, and differentiation. Which of the following viruses most likely caused this patient's in utero infection?

A. Cytomegalovirus
B. Herpes simplex virus
C. Parvovirus B19
D. Rubella virus
E. Varicella zoster virus

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The patient spontaneously delivers a stillborn fetus with multiple congenital malformations. Fetal autopsy reveals microcephaly with thin cerebral cortices, ventriculomegaly, and subcortical calcifications. Viral RNA of a neurotropic virus is detected in body fluids of the mother and the fetus. Transplacental transmission of this virus causes apoptosis of neural progenitor cells in the developing fetus, leading to disruption of neuronal proliferation, migration, and differentiation. Which of the following viruses most likely caused this patient's in utero infection?

A. Cytomegalovirus
B. Herpes simplex virus
C. Parvovirus B19
D. Rubella virus
E. Varicella zoster virus
F. Zika virus

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The patient spontaneously delivers a stillborn fetus with multiple congenital malformations. Fetal autopsy reveals microcephaly with thin cerebral cortices, ventriculomegaly, and subcortical calcifications. Viral RNA of a neurotropic virus is detected in body fluids of the mother and the fetus. Transplacental transmission of this virus causes apoptosis of neural progenitor cells in the developing fetus, leading to disruption of neuronal proliferation, migration, and differentiation. Which of the following viruses most likely caused this patient's in utero infection?

A. ~~Cytomegalovirus~~ (25%)
B. ~~Herpes simplex virus~~ (1%)
C. Parvovirus B19 (4%)
D. ~~Rubella virus~~ (13%)
E. ~~Varicella zoster virus~~ (1%)
✓ F. Zika virus (53%)

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53%
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Congenital Zika syndrome	
Pathogenesis	• Single-stranded RNA *Flavivirus* • Transplacental transmission to fetus • Targets neural progenitor cells
Clinical features	• Microcephaly, craniofacial disproportion • Neurologic abnormalities (eg, spasticity, seizures) • Ocular abnormalities
Diagnosis	• Neuroimaging: Calcifications, ventriculomegaly, cortical thinning • Zika RNA detection

Zika virus is a **single-stranded RNA** virus belonging to the *Flavivirus* genus. Transmission occurs primarily via an *Aedes* mosquito bite, but infected patients can also spread the virus via genital secretions. The neurotropic virus can cross the placenta and infect and destroy **fetal neural progenitor cells**, causing congenital Zika syndrome and possible fetal demise. Fetal brain development is impaired due to disruption of normal proliferation, migration, and differentiation of neurons.

Classic findings in affected newborns include **microcephaly** with facial features out of proportion to head

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Classic findings in affected newborns include **microcephaly** with facial features out of proportion to head size, **arthrogryposis** (contractures), seizures, hypertonia, and ocular abnormalities. Loss of brain mass (eg, **cortical thinning**, ventriculomegaly) as well as subcortical calcifications are typically present. Diagnosis is confirmed by detection of Zika RNA (real-time reverse transcriptase PCR) in serum, urine, or cerebrospinal fluid.

The mainstay of treatment for surviving infants is supportive care with management of feeding difficulties, hydrocephalus, and seizures. Pregnant women should be counseled to avoid traveling to areas with ongoing Zika transmission (eg, South and Central America, Asia, Africa, Mexico, the Caribbean).

(Choices A, B, and E) Cytomegalovirus (CMV), herpes simplex virus (HSV), and varicella zoster virus (VZV) are double-stranded DNA viruses that can be transmitted in utero and cause CNS abnormalities in the fetus. Typical CMV findings include hearing loss, chorioretinitis, jaundice, and periventricular calcifications. When transmitted in utero, HSV and VZV can cause diffuse cutaneous lesions and severe brain destruction; hypoplasia of the limbs and eyes is also commonly seen with fetal VZV infection.

(Choice C) Parvovirus B19 is a single-stranded DNA virus that infects and destroys erythroid progenitor cells and can result in fetal hydrops when the infection is contracted during pregnancy.

(Choice D) Rubella virus is a single-stranded RNA virus that typically presents with cardiac defects.

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(Choice D) Rubella virus is a single-stranded RNA virus that typically presents with cardiac defects, hearing loss, and cataracts.

Educational objective:
Zika virus is a single-stranded RNA virus that infects fetal neural progenitor cells, causing severe congenital malformations (eg, microcephaly, arthrogryposis), cerebral cortical thinning, and possible fetal demise.

References

- Congenital Zika virus infection: beyond neonatal microcephaly.
- Zika virus infection.

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Correct

53%
Answered correctly

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Explanation

Congenital Zika syndrome	
Pathogenesis	• Single-stranded RNA *Flavivirus* • Transplacental transmission to fetus • Targets neural progenitor cells
Clinical features	• Microcephaly, craniofacial disproportion • Neurologic abnormalities (eg, spasticity, seizures) • Ocular abnormalities
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- Zika RNA detection

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Educational objective:
Zika virus is a single-stranded RNA virus that infects fetal neural progenitor cells, causing severe congenital malformations (eg, microcephaly, arthrogryposis), cerebral cortical thinning, and possible fetal demise.

References

- Congenital Zika virus infection: beyond neonatal microcephaly.

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A 5-year-old boy is brought to the emergency department with worsening somnolence, lethargy, and decreased urine output. The patient has no prior medical conditions but had abdominal cramps and diarrhea several days ago that later became frankly bloody. Physical examination shows mild pallor and moist mucous membranes. Laboratory studies reveal elevated blood urea nitrogen and serum creatinine levels. Peripheral blood smear shows fragmented erythrocytes. This patient's condition is most likely related to consumption of which of the following foods?

- A. Canned beans
- B. Custard
- C. Fried rice
- D. Mayonnaise
- E. Oysters
- F. Raw eggs
- G. Undercooked beef

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decreased urine output. The patient has no prior medical conditions but had abdominal cramps and diarrhea several days ago that later became frankly bloody. Physical examination shows mild pallor and moist mucous membranes. Laboratory studies reveal elevated blood urea nitrogen and serum creatinine levels. Peripheral blood smear shows fragmented erythrocytes. This patient's condition is most likely related to consumption of which of the following foods?

- A. Canned beans (9%)
- B. Custard (1%)
- C. Fried rice (2%)
- D. Mayonnaise (4%)
- E. Oysters (4%)
- F. Raw eggs (4%)
- ✓ G. Undercooked beef (73%)

Correct

73%

36 secs

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Hemolytic uremic syndrome	
Etiology	Shiga toxin-producing bacteria • *Escherichia coli* O157:H7 • *Shigella*
Clinical features	• Antecedent diarrheal illness (often bloody) • Hemolytic anemia with schistocytes • Thrombocytopenia • Acute kidney injury

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Hemolytic uremic syndrome (HUS) is a major cause of acute renal failure in children. It is characterized by the triad of renal insufficiency, thrombocytopenia, and microangiopathic hemolytic anemia. Most cases occur due to underlying **enterohemorrhagic *Escherichia coli*** (EHEC) infection, particularly with the O157:H7 serotype.

EHEC is a gram-negative, enteric rod that acquires the ability to produce **Shiga toxin** from a lysogenic bacteriophage. Shiga toxin enters the cytosol of host cells and cleaves a protein motif off the 60S ribosomal subunit, which irreversibly halts host protein synthesis and causes cell death. Toxin-mediated

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EHEC is a gram-negative, enteric rod that acquires the ability to produce **Shiga toxin** from a lysogenic bacteriophage. Shiga toxin enters the cytosol of host cells and cleaves a protein motif off the 60S ribosomal subunit, which irreversibly halts host protein synthesis and causes cell death. Toxin-mediated injury to the colonic mucosa and the colonic capillaries causes abdominal pain and **bloody diarrhea**. The absorption of Shiga toxin into the systemic circulation causes glomerular (renal insufficiency) and vascular (thrombocytopenia, microangiopathic hemolytic anemia) injury in a minority of patients, leading to HUS.

The primary reservoir for EHEC is the gastrointestinal tract of healthy cattle. Humans primarily acquire the organism after consuming contaminated, **undercooked beef**. Because low infectious doses (10-100 organisms) are required for disease, meatpacking facilities that process high volumes of ground beef are an important source of outbreaks. Other less common routes of transmission include person-to-person contact and fruits and vegetables contaminated with manure.

(Choice A) Canned foods that are contaminated with *Clostridium botulinum* can be associated with foodborne illness due to the consumption of preformed botulism toxin. Patients typically develop descending, symmetric paralysis.

(Choices B and D) The consumption of preformed, heat-stable *Staphylococcus aureus* enterotoxin causes self-limited nausea, vomiting, and abdominal cramping 1-6 hours after ingestion. Dairy (eg, custard), produce, meats, eggs (eg, mayonnaise), and salads are common culprits and are usually

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(Choices B and D) The consumption of preformed, heat-stable *Staphylococcus aureus* enterotoxin causes self-limited nausea, vomiting, and abdominal cramping 1-6 hours after ingestion. Dairy (eg, custard), produce, meats, eggs (eg, mayonnaise), and salads are common culprits and are usually inoculated during preparation by a food handler.

(Choice C) *Bacillus cereus* enterotoxin is classically associated with reheated rice. It causes a vomiting-predominant, foodborne illness that clinically resembles the illness seen with *S aureus* enterotoxin.

(Choice E) Consumption of raw oysters can lead to infection with *Vibrio parahaemolyticus* (which causes voluminous watery diarrhea similar to cholera) and *Vibrio vulnificus* (which causes sepsis with high mortality), as well as other *Vibrio* infections.

(Choice F) The consumption of raw eggs or incompletely cooked poultry can lead to *Salmonella* gastroenteritis, which usually causes watery diarrhea, abdominal cramping, vomiting, and fever.

Educational objective:
Enterohemorrhagic *Escherichia coli* (EHEC) is primarily contracted after eating undercooked ground beef. EHEC produces Shiga toxin, which causes hemorrhagic colitis and can lead to hemolytic-uremic syndrome (HUS). HUS is characterized by acute renal failure, thrombocytopenia, and microangiopathic hemolytic anemia; children age <10 are at greatest risk.

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Three cases of severe pharyngitis were reported in a community of immigrants. The patients had thick pharyngeal exudates, neck swelling, and difficulty swallowing. One of them died from severe heart failure. The toxin responsible has a mechanism of action most similar to another toxin produced by which of the following bacteria?

A. *Pseudomonas aeruginosa*
B. *Staphylococcus aureus*
C. *Clostridium difficile*
D. *Clostridium botulinum*
E. *Bordetella pertussis*
F. *Vibrio cholerae*

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Three cases of severe pharyngitis were reported in a community of immigrants. The patients had thick pharyngeal exudates, neck swelling, and difficulty swallowing. One of them died from severe heart failure. The toxin responsible has a mechanism of action most similar to another toxin produced by which of the following bacteria?

- A. *Pseudomonas aeruginosa* (57%)
- B. *Staphylococcus aureus* (9%)
- C. *Clostridium difficile* (7%)
- D. *Clostridium botulinum* (3%)
- E. *Bordetella pertussis* (16%)
- F. *Vibrio cholerae* (4%)

Correct

57% Answered correctly

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Severe pharyngitis with exudates and cervical lymphadenopathy in a group of people with unknown vaccination status should raise suspicion for respiratory diphtheria infection. Diphtheria toxin can cause severe myocarditis and heart failure, which occurred in one of the patients in the vignette. Diphtheria toxin acts in a similar manner to exotoxin A, which is produced by *Pseudomonas aeruginosa*.

P aeruginosa produces several extracellular products, including exotoxin A, collagenase, elastase, fibrinolysin, phospholipase C, and DNAse. These substances assist in its invasion and dissemination in human tissues. Although they are structurally different, both diphtheria toxin and exotoxin A ribosylate and inactivate elongation factor-2 (EF-2), halting human cell protein synthesis and causing cell death. Exotoxin A is a major virulence factor and is responsible for the high mortality associated with *P aeruginosa* septicemia.

Mechanism of action of bacterial toxins

Choice	Organism	Toxin	Microbiology
	C. diphtheriae	Diphtheria toxin	Inactivates EF-2 via ribosylation, thus inhibiting host cell protein synthesis

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Choice	Organism	Toxin	Microbiology
	C. diphtheriae	Diphtheria toxin	Inactivates EF-2 via ribosylation, thus inhibiting host cell protein synthesis
A	*P. aeruginosa*	Exotoxin A	Inactivates EF-2 via ribosylation, thus inhibiting host cell protein synthesis
B	*S. aureus*	Enterotoxin	Superantigen that acts locally in the GI tract causing vomiting
		TSS toxin	Superantigen that stimulates T-cells leading to widespread cytokine release and shock
C	*C. difficile*	Cytotoxin B	Induces actin depolymerization leading to mucosal cell death, necrosis of colonic mucosal surfaces, & pseudomembrane formation
D	*C. botulinum*	Botulinum toxin	Blocks the presynaptic release of acetycholine at the neuromuscular junction resulting in flaccid paralysis
			Disinhibits adenylate cyclase via G_i ADP

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D	*C. botulinum*	Botulinum toxin	at the neuromuscular junction resulting in flaccid paralysis
E	*B. pertussis*	Pertussis toxin	Disinhibits adenylate cyclase via G_i ADP ribosylation, increasing cAMP production in the host cell; causes increased histamine sensitivity & phagocyte dysfunction
F	*V. cholerae*	Cholera toxin	Activates adenylate cyclase via G_s ADP ribosylation, increasing cAMP production in the host cell; causes secretory diarrhea, dehydration, & electrolyte imbalances

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Educational objective:

Diphtheria toxin and pseudomonal exotoxin A act by ribosylating and inactivating elongation factor-2, inhibiting host cell protein synthesis and causing cell death.

Microbiology	Infectious Diseases	Diphtheria
Subject	System	Topic

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A 24-year-old man comes to the emergency department with leg swelling. His dog, which is fully vaccinated and has lived with him for the past year, bit him on the left leg last night, leading to a break in the skin and bleeding. The patient irrigated the wound with bottled water and soap and managed his pain with acetaminophen. This morning, the wound area became warm, red, and swollen. On examination, temperature is 36.4 C (97.5 F). There is an open wound on the left leg, with surrounding erythema, warmth, and tenderness. No wound drainage or crepitus is present. The distal pulses are palpable. Wound cultures grow gram-negative coccobacilli; the culture has a mouse-like odor. Which of the following organisms is most likely responsible for this patient's current presentation?

- A. *Bartonella henselae*
- B. *Campylobacter jejuni*
- C. *Clostridium perfringens*
- D. *Coxiella burnetii*
- E. *Erysipelothrix rhusiopathiae*
- F. *Francisella tularensis*

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- D. *Coxiella burnetii*
- E. *Erysipelothrix rhusiopathiae*
- F. *Francisella tularensis*
- G. *Fusobacterium*
- H. *Pasteurella multocida*
- I. *Proteus mirabilis*

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warmth, and tenderness. No wound drainage or crepitus is present. The distal pulses are palpable.

Wound cultures grow gram-negative coccobacilli; the culture has a mouse-like odor. Which of the following organisms is most likely responsible for this patient's current presentation?

A. *Bartonella henselae* (7%)
B. ~~*Campylobacter jejuni*~~ (1%)
C. ~~*Clostridium perfringens*~~ (2%)
D. ~~*Coxiella burnetii*~~ (2%)
E. ~~*Erysipelothrix rhusiopathiae*~~ (1%)
F. ~~*Francisella tularensis*~~ (3%)
G. ~~*Fusobacterium*~~ (1%)
✓ H. *Pasteurella multocida* (77%)
I. ~~*Proteus mirabilis*~~ (1%)

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Microbiology of human & animal bites	
Cat bite	• *Pasteurella multocida* (most common) • *Bartonella henselae* (lymphangitis in immunocompetent hosts)
Dog bite	• *Pasteurella multocida* • Streptococci • *Staphylococcus aureus*
Human bite	• Anaerobes • Streptococci • *Eikenella corrodens*: Clenched-fist injury ("fight bite")

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This patient has a skin and soft-tissue infection (SSTI) that developed at the site of a dog bite relatively soon following the bite. ***Pasteurella multocida*** is an organism found in the mouths of dogs and is responsible for the majority of acute skin infections following a **dog bite**. Infection typically occurs **within 24 hours** of inoculation and has a characteristic **mouse-like** odor (indole-positive species). *P multocida*

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24 hours of inoculation and has a characteristic **mouse-like** odor (indole-positive species). *P multocida* SSTI can also occur following a cat bite. Other organisms associated with dog bites include staphylococci, streptococci, and *Capnocytophaga canimorsus*. Management includes wound care and antibiotics (eg, amoxicillin-clavulanate).

(Choice A) *Bartonella henselae* is associated with cat-scratch disease, which can develop following inoculation from an infected cat and presents with lymphadenopathy that is often self-limiting. It is not associated with dog bites.

(Choices B and I) *Campylobacter jejuni* typically causes gastrointestinal (diarrheal) illness, and *Proteus mirabilis* is a common cause of urinary tract infection.

(Choices C and E) *Clostridium perfringens* is an anaerobe that can cause necrotizing SSTI, which occurs most commonly after a traumatic wound and leads to myonecrosis and gas gangrene. *Erysipelothrix rhusiopathiae* is a gram-positive rod (not a gram-negative coccobacillus) that causes erysipeloid.

(Choices D and G) *Coxiella burnetii* can cause Q fever, a mild form of pneumonia. *Fusobacterium* is part of the anaerobic oral flora potentially causing aspiration pneumonia or pharyngitis (Lemierre disease).

(Choice F) *Francisella tularensis* causes tularemia, a zoonotic infection that can occur following contact with lagomorphs and rodents (eg, rabbits, beavers, squirrels). The presentation is variable (eg, severe

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most commonly after a traumatic wound and leads to myonecrosis and gas gangrene. *Erysipelothrix rhusiopathiae* is a gram-positive rod (not a gram-negative coccobacillus) that causes erysipeloid.

(Choices D and G) *Coxiella burnetii* can cause Q fever, a mild form of pneumonia. *Fusobacterium* is part of the anaerobic oral flora potentially causing aspiration pneumonia or pharyngitis (Lemierre disease).

(Choice F) *Francisella tularensis* causes tularemia, a zoonotic infection that can occur following contact with lagomorphs and rodents (eg, rabbits, beavers, squirrels). The presentation is variable (eg, severe febrile pulmonary infection, ulcerative disease at inoculation site).

Educational objective:

Pasteurella multocida is a cause of soft-tissue infection that develops within 24 hours following a dog or cat bite. Management includes wound care and antibiotics targeted against this organism.

References

- Dog and cat bites.
- Bite wounds and infection.

Microbiology	Infectious Diseases	Animal and human bite injuries
Subject	System	Topic

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A neonate born to a 26-year-old woman is evaluated in the newborn nursery. The patient was delivered vaginally at 38 weeks gestation, and Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. Initial evaluation shows hydrocephalus, jaundice, and hepatosplenomegaly. Funduscopic examination reveals retinal exudates and scarring. Histopathologic evaluation of the placenta shows infiltration of lymphocytes, plasma cells, and macrophages, as well as many areas of calcification. Within the placental tissue, there are numerous intracellular, crescent-shaped organisms with a central nucleus. Which of the following maternal interventions would have been most effective in preventing this patient's condition?

A. Adequate preconception immunization
B. Avoidance of consumption of undercooked meat
C. Consumption of unpasteurized cow's milk products
D. Strict avoidance of mosquitoes during pregnancy
E. Use of prophylactic penicillin during labor

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A. Adequate preconception immunization (16%)
B. Avoidance of consumption of undercooked meat (54%)
C. Consumption of unpasteurized cow's milk products (9%)
D. Strict avoidance of mosquitoes during pregnancy (14%)
E. Use of prophylactic penicillin during labor (5%)

54% 03 mins, 33 secs 12/14/2020

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Congenital toxoplasmosis	
Pathogenesis	• *Toxoplasma gondii* infection in cats (definitive host) • Spread to humans & animals via oocysts shed in cat feces • Transplacental transmission from infected mother to fetus
Maternal risk factors	• Raw or undercooked meat (infected farm animals) • Unwashed produce (contaminated soil) • Handling of cat feces
Clinical features	• Chorioretinitis* • Diffuse intracranial calcifications* • Microcephaly (brain atrophy) or macrocephaly (hydrocephalus*) • Nonspecific: jaundice, hepatosplenomegaly

*Classic triad of clinical features.

This neonate with retinal lesions (**chorioretinitis**) and **hydrocephalus** has a placenta containing inflammatory cells, calcifications, and **crescent-shaped organisms**. These findings are consistent with

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This neonate with retinal lesions (**chorioretinitis**) and **hydrocephalus** has a placenta containing inflammatory cells, calcifications, and **crescent-shaped organisms**. These findings are consistent with **congenital toxoplasmosis**, an infection caused by the intracellular parasite *Toxoplasma gondii*. Nonspecific neonatal findings of jaundice and hepatosplenomegaly are often present; **diffuse intracranial calcifications** are the classic finding on imaging.

Parasitic spread of *Toxoplasma* begins via infected cats (host), which excrete oocysts that contaminate soil and water. Humans typically acquire the infection due to either of the following:

- Incidental ingestion of oocysts from **cat feces** (eg, handling kitty litter, consuming unwashed produce)
- Consumption of **undercooked meat** from farm animals that ingested oocysts and developed tissue infection

Ingestion of contaminated meat is the most common method of spread in pregnancy. Therefore, although maternal infection is often asymptomatic, pregnant women are advised to **avoid** raw, cured, and undercooked meat to reduce the risk of infection and transplacental transmission to the fetus.

(Choice A) Preconception maternal immunization with the measles, mumps, and rubella vaccine can prevent congenital rubella infection. Characteristic features of congenital rubella include hearing loss,

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(Choice A) Preconception maternal immunization with the measles, mumps, and rubella vaccine can prevent congenital rubella infection. Characteristic features of congenital rubella include hearing loss, cataracts (cloudy cornea), and cardiac defects (eg, patent ductus arteriosus), none of which are seen in this patient. Moreover, retinal lesions and hydrocephalus are uncommon, and rubella is a virus, not a crescent-shaped, intracellular parasite.

(Choice C) Pregnant women should avoid, not preferentially consume, unpasteurized milk products, primarily to prevent congenital *Listeria monocytogenes* infection, which can lead to multiorgan abscesses or fetal demise. Although rare, *Toxoplasma* and other pathogens can also spread through raw milk.

(Choice D) Malaria, a parasitic infection transmitted by mosquitoes, can cause intrauterine infection, but infants with congenital malaria typically present with fever and anemia, not hydrocephalus and chorioretinitis. In addition, although *Plasmodium falciparum* is a crescent-shaped intracellular organism, placental biopsy would show intervillous accumulation of parasitized red blood cells without calcifications.

(Choice E) Prophylactic penicillin is used during labor to prevent group B *Streptococcus* (GBS) transmission to the fetus during delivery. Infection typically leads to early neonatal sepsis (eg, lethargy, hypoxia, temperature instability), findings not seen in this patient. Moreover, in contrast to this patient's pathologic findings, GBS is a gram-positive coccus that forms chains

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(Choice D) Malaria, a parasitic infection transmitted by mosquitoes, can cause intrauterine infection, but infants with congenital malaria typically present with fever and anemia, not hydrocephalus and chorioretinitis. In addition, although *Plasmodium falciparum* is a crescent-shaped intracellular organism, placental biopsy would show intervillous accumulation of parasitized red blood cells without calcifications.

(Choice E) Prophylactic penicillin is used during labor to prevent group B *Streptococcus* (GBS) transmission to the fetus during delivery. Infection typically leads to early neonatal sepsis (eg, lethargy, hypoxia, temperature instability), findings not seen in this patient. Moreover, in contrast to this patient's pathologic findings, GBS is a gram-positive coccus that forms chains.

Educational objective:

Pregnant women should avoid consumption of undercooked meat to prevent infection with *Toxoplasma gondii*, an intracellular, crescent-shaped parasite that can cross the placenta to the fetus. Typical features of congenital toxoplasmosis include chorioretinitis, hydrocephalus, and diffuse intracranial calcifications.

Microbiology	Infectious Diseases	Toxoplasmosis
Subject	System	Topic

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A 13-year-old boy is brought to the clinic by his parents due to a change in behavior. His special education teacher reported that for the last several weeks he has frequently taken off his shoes to scratch his feet during class. The patient has a history of learning disability but is otherwise healthy. Examination shows erythema and excoriations between the toes of both feet. Microscopy of skin scrapings from the rash is shown in the exhibit. Which of the following antimicrobial drugs is likely to be the most effective against the pathogen causing this patient's condition?

A. Albendazole
B. Clotrimazole
C. Mupirocin
D. Nystatin
E. Permethrin

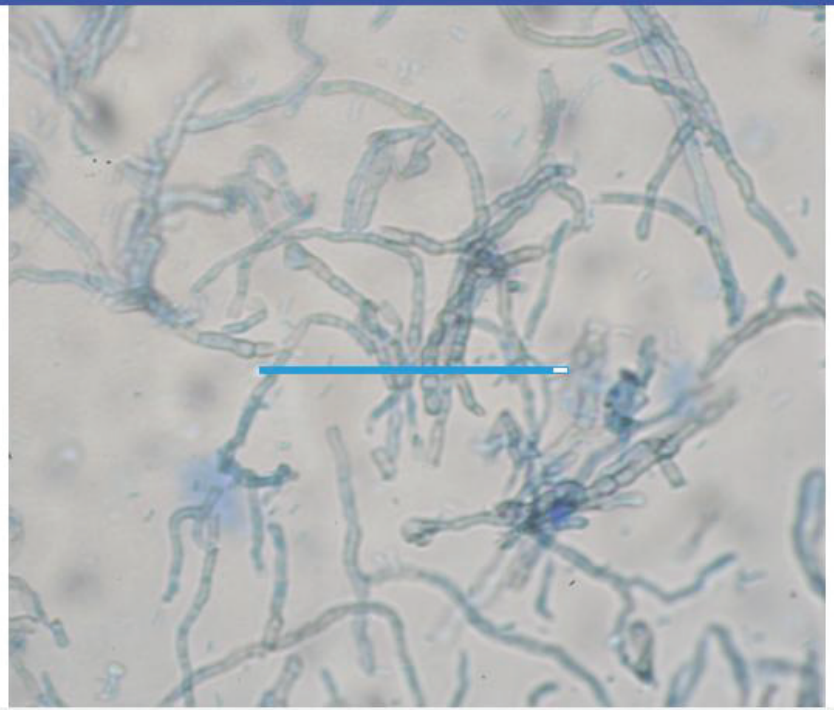
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Exhibit Display



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A. Albendazole (8%)
B. Clotrimazole (61%)
C. Mupirocin (2%)
D. Nystatin (18%)
E. Permethrin (8%)

Correct

61%
Answered correctly

12 mins, 05 secs
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Tinea pedis	
Etiology	• *Trichophyton* species (most common)
Clinical features	• Pruritus, erythema, erosions/scaling • Most often interdigital or covering the sole (moccasin type) • Segmented hyphae on KOH preparation
Treatment	• Topical antifungal therapy (eg, azoles, terbinafine) • Keep feet dry & dispose of old footwear

This patient has a pruritic, erythematous rash affecting the feet. Microscopy of skin scrapings shows

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	footwear

This patient has a pruritic, erythematous rash affecting the feet. Microscopy of skin scrapings shows branching hyphae, confirming the diagnosis of **tinea pedis** (athlete's foot). Tinea pedis is a superficial infection of the epidermis caused by **dermatophytes**, especially *Trichophyton rubrum* and similar species. The organisms are widespread and are often acquired following exposure to public places while barefoot (eg, athletic facilities, swimming pools). They can also spread from other areas (eg, groin [tinea cruris], body [tinea corporis]) on the same patient via autoinoculation.

Tinea pedis most commonly occurs between the toes (interdigital pattern) but in chronic cases can cause a hyperkeratotic rash extending up the sides of the feet (moccasin pattern). Tinea pedis is treated with a variety of **topical antifungals**, including azoles (eg, miconazole, **clotrimazole**), allylamines (eg, terbinafine), and tolnaftate. However, nystatin (primarily used for *Candida* infections) is not effective against dermatophytes **(Choice D)**.

(Choice A) Albendazole is an antihelminthic agent used to treat cutaneous larva migrans, which presents with pruritic, red/brown serpiginous tracks in the skin. The feet are typically the initial location of infection, but symptoms would not be confined to the interdigital skin.

(Choice C) Topical mupirocin is used to treat impetigo, which presents with well-defined erythematous,

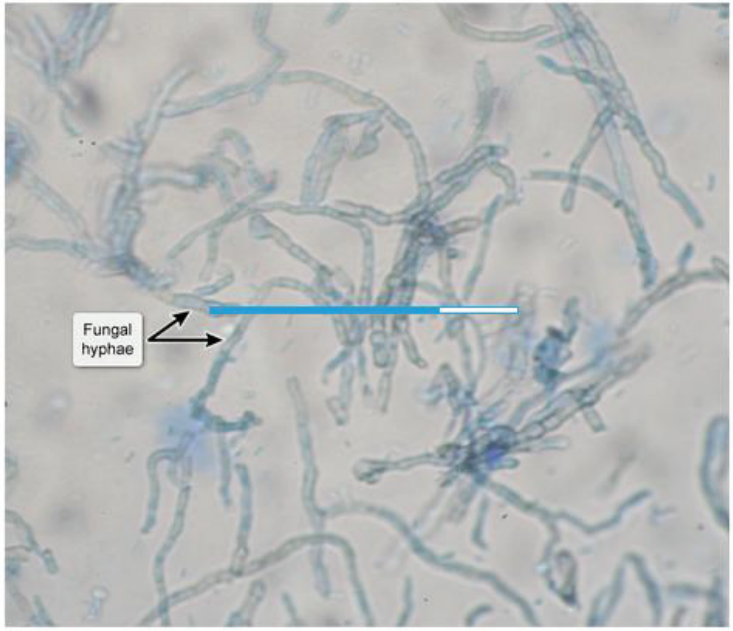
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Exhibit Display

Tinea pedis



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[Choice C] Topical mupirocin is used to treat impetigo, which presents with well-defined erythematous

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Exhibit Display

Tinea pedis



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(Choice C) Topical mupirocin is used to treat impetigo, which presents with well-defined erythematous

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Exhibit Display

Cutaneous larva migrans



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[Choice C] Topical mupirocin is used to treat impetigo, which presents with well-defined erythematous

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against dermatophytes **(Choice D)**.

(Choice A) Albendazole is an antihelminthic agent used to treat cutaneous larva migrans, which presents with pruritic, red/brown serpiginous tracks in the skin. The feet are typically the initial location of infection, but symptoms would not be confined to the interdigital skin.

(Choice C) Topical mupirocin is used to treat impetigo, which presents with well-defined erythematous, erosive lesions with yellow crust.

(Choice E) Permethrin is used for scabies, which can affect the interdigital skin but presents with small papules, pustules, and burrows. Microscopy of skin scrapings shows mites or ova and fecal matter.

Educational objective:

Tinea pedis is a superficial infection of the epidermis caused by dermatophytes (eg, *Trichophyton rubrum*). It most often presents as a pruritic, erythematous rash between the toes that frequently extends along the sole. Microscopy of skin scrapings shows branching hyphae. Treatment options include a variety of topical antifungals (eg, clotrimazole), but not nystatin.

Pharmacology	Infectious Diseases	Tinea
Subject	System	Topic

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against dermatophytes **(Choice D)**.

Exhibit Display

Scabies



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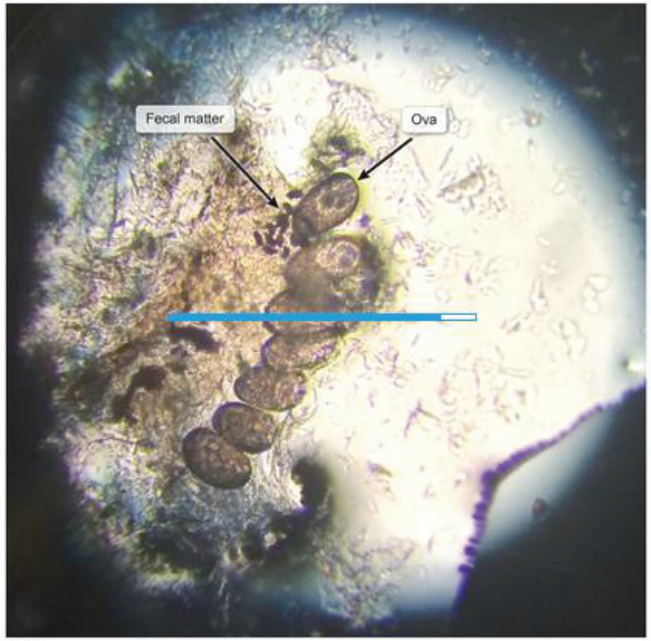
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against dermatophytes **(Choice D)**.

Exhibit Display

Scabies



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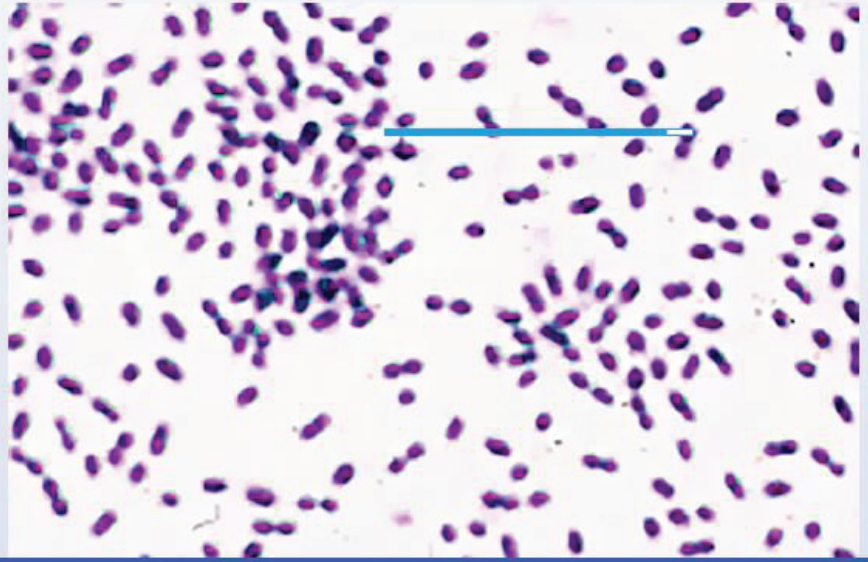
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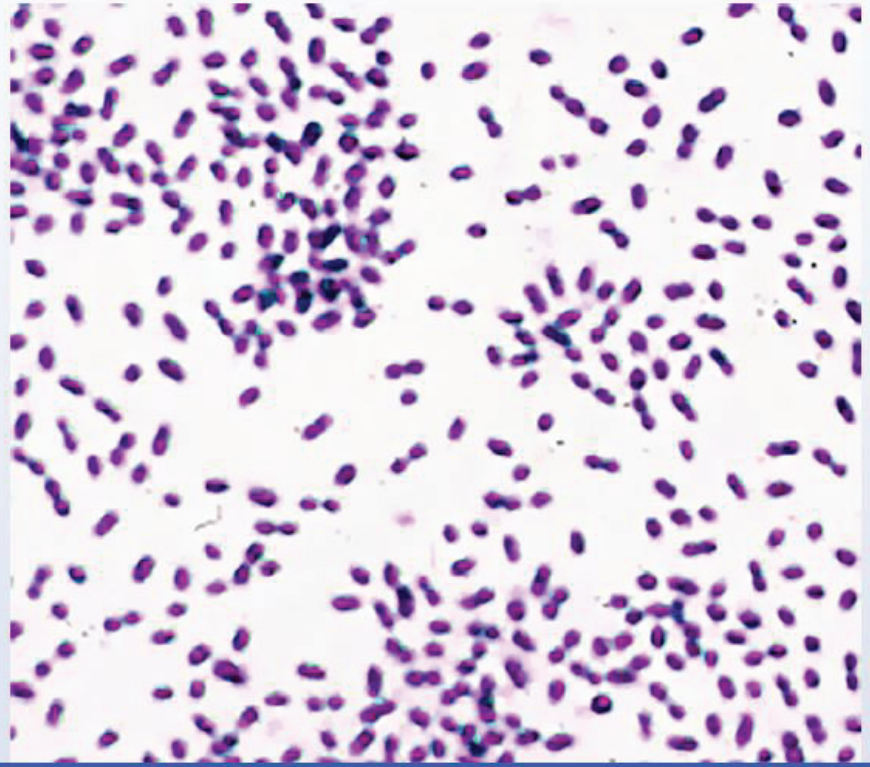
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A 40-year-old woman comes to the emergency department due to malaise, fever, productive cough, and pleuritic chest pain. The patient has a history of alcohol abuse and HIV acquired from injection drug use. She is nonadherent with antiretroviral therapy and other HIV-related medications. Temperature is 38.3 C (101 F), blood pressure is 120/72 mm Hg, and pulse is 104/min. Lung examination reveals bronchial breath sounds and crackles. Sputum microscopy findings are shown below.



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(101°F), blood pressure is 120/72 mm Hg, and pulse is 104/min. Lung examination reveals bronchial breath sounds and crackles. Sputum microscopy findings are shown below.



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Which of the following pathogenic factors most likely contributes to this microorganism's ability to cause lung infection?

A. Alveolar hyaline membrane formation

B. Antiphagocytic microbial capsule

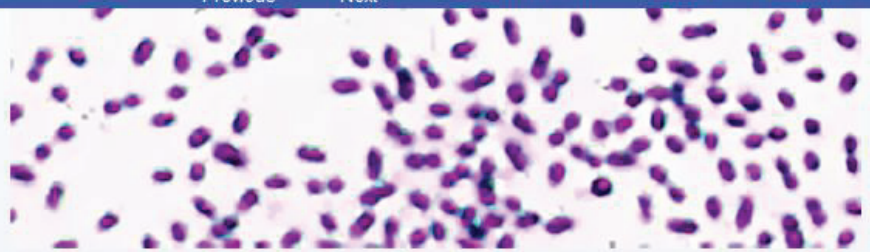
C. Endotoxin-induced cell necrosis

D. Intracytoplasmic location of the organism

E. Lipid-rich microbial cell wall

Submit

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Which of the following pathogenic factors most likely contributes to this microorganism's ability to cause lung infection?

A. ~~Alveolar hyaline membrane formation~~ (3%)
B. Antiphagocytic microbial capsule (71%)
C. Endotoxin-induced cell necrosis (3%)
D. Intracytoplasmic location of the organism (11%)
E. Lipid-rich microbial cell wall (9%)

Correct

71%

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Streptococcus pneumoniae is a gram-positive, lancet-shaped organism that grows in pairs (diplococci). It colonizes the nasopharynx and is a leading cause of **community-acquired pneumonia**, bacterial meningitis, sinusitis, otitis media, and sepsis. Patients with HIV have increased susceptibility, as the virus dramatically hampers the production of opsonizing antibodies and the recruitment of phagocytes to areas of infection.

The major virulence factor of *S pneumoniae* is a thick **polysaccharide capsule**, which impedes phagocytosis and complement binding. Antibodies against the capsule form during infection and are protective against future infections with that strain. However, over 90 capsular serotypes have been identified. Therefore, patients at high risk of pneumococcal infection (eg, **HIV**, extremes of age) should receive the pneumococcal vaccine, which contains polysaccharide antigens from the most common strains.

Other S *pneumoniae* virulence factors include IgA protease (inactivates secretory IgA), adhesins (necessary for adhesion to epithelial cells), and pneumolysin (a cytotoxin that causes pores in cell membranes and cell lysis).

(Choice A) Alveolar hyaline membranes are fibrinous deposits that line the alveoli and inhibit gas transfer. They usually result in significant dyspnea and/or respiratory collapse, and are typically seen with infantile respiratory distress syndrome and acute respiratory distress syndrome.

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They usually result in significant dyspnea and/or respiratory collapse, and are typically seen with infantile respiratory distress syndrome and acute respiratory distress syndrome.

(Choice C) Endotoxins (eg, lipopolysaccharide) are found in the outer membrane of gram-negative pathogens (eg, *Neisseria*) and produce a strong inflammatory response when released into the circulation. Gram-positive organisms do not have endotoxins but some release exotoxins.

(Choice D) Intracellular organisms such as *Neisseria*, *Listeria*, and *Mycobacterium tuberculosis* are protected from immunoglobulin and complement binding. *S pneumoniae* is an extracellular pathogen.

(Choice E) *Mycobacteria* have lipid-rich mycolic acid in their cell walls, which causes them to be acid-fast. Mycolic acids inhibit bacterial destruction by the phagolysosome and contribute to granuloma formation.

Educational objective:
The virulence of *Streptococcus pneumoniae* is predominantly due to its polysaccharide capsule, which impedes phagocytosis and complement binding.

Microbiology	Infectious Diseases	Community acquired pneumonia
Subject	System	Topic

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A 23-year-old woman is brought to the emergency department due to one day of fever, vomiting, diarrhea, and muscle pains. The symptoms developed rapidly over the course of the day. The patient is confused and unable to answer questions. She has no known medical problems and takes no medications. She lives with her boyfriend. The patient's temperature is 39.1 C (102.4 F), blood pressure is 88/50 mm Hg, pulse is 120/min, and respirations are 20/min. A diffuse, erythematous, macular rash resembling a sunburn is noted on dermatologic examination; pelvic examination reveals a tampon in the vagina. Laboratory results are as follows:

Leukocytes	8,000/mm^3
Creatinine	1.4 mg/dL
Aspartate aminotransferase (SGOT)	62 U/L
Alanine aminotransferase (SGPT)	49 U/L

A pregnancy test is negative. Activation of which of the following cells is most likely primarily responsible

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Aspartate aminotransferase (SGOT)	62 U/L
Alanine aminotransferase (SGPT)	49 U/L

A pregnancy test is negative. Activation of which of the following cells is most likely primarily responsible for this patient's condition?

A. Basophils and macrophages
B. Macrophages and T lymphocytes
C. Mast cells and eosinophils
D. Neutrophils and B lymphocytes
E. Platelets and mast cells

Submit

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Aspartate aminotransferase (SGOT)	62 U/L
Alanine aminotransferase (SGPT)	49 U/L

A pregnancy test is negative. Activation of which of the following cells is most likely primarily responsible for this patient's condition?

- A. Basophils and macrophages (3%)
- ✓ B. Macrophages and T lymphocytes (67%)
- C. Mast cells and eosinophils (11%)
- D. Neutrophils and B lymphocytes (12%)
- E. Platelets and mast cells (5%)

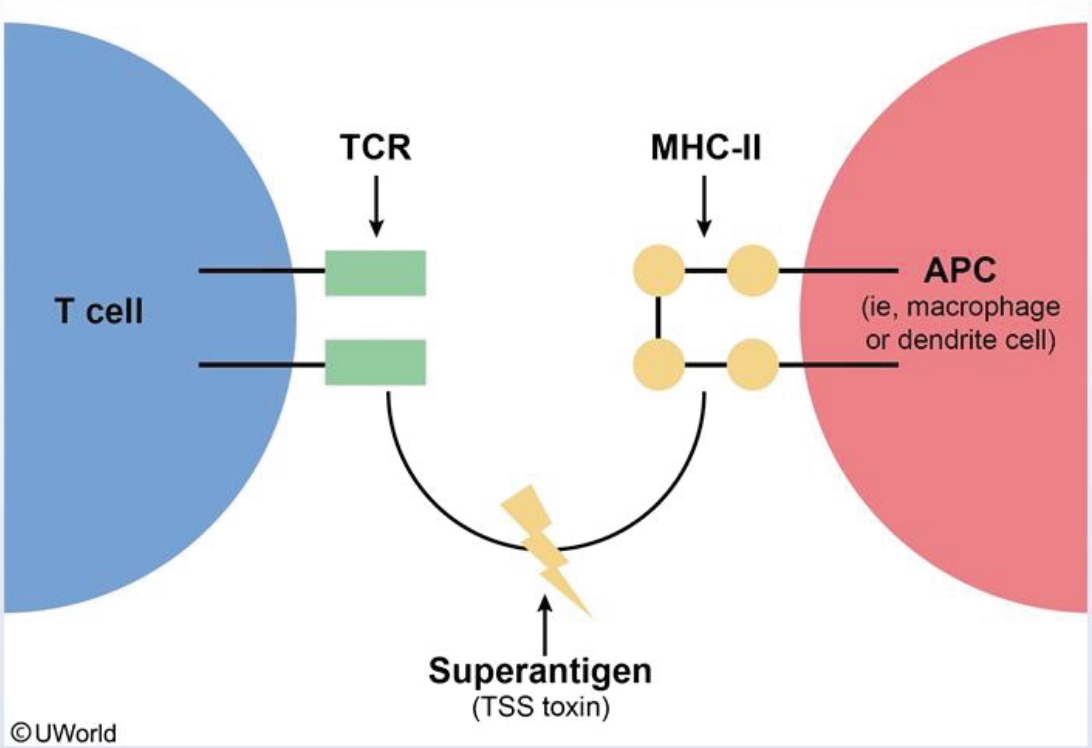
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67%
Answered correctly

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Fever, vomiting, diarrhea, muscle pains, and erythroderma (diffuse macular rash resembling a sunburn) are

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(TSS toxin)

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Fever, vomiting, diarrhea, muscle pains, and erythroderma (diffuse macular rash resembling a sunburn) are manifestations of **toxic shock syndrome (TSS)**. TSS can rapidly progress to severe hypotension and multisystem dysfunction (eg, elevated creatinine, elevated transaminases). Desquamation, particularly on the palms and soles, can occur 1-2 weeks after the onset of illness. TSS has been associated with the use of **tampons** and nasal packing.

Staphylococcus aureus strains producing **toxic shock syndrome toxin** (TSST) are responsible for most cases of TSS. TSST acts as a **superantigen** that activates large numbers of helper T cells (compared to a regular antigen, which activates few helper T cells). Superantigens interact with major histocompatibility complex molecules on antigen-presenting cells (eg, **macrophages**) and with the variable region of the **T lymphocyte** receptor to cause a nonspecific, **widespread** activation of T lymphocytes. Activation of T cells is responsible for the release of interleukin (IL)-2 from the T cells and IL-1 and tumor necrosis factor from macrophages. These ILs cause capillary leakage, circulatory collapse, hypotension, shock, fever, skin findings, and multiorgan failure.

(Choice A) Basophils are not involved in TSS. Basophilia can be seen with some myeloproliferative disorders and, rarely, certain parasitic infections.

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(Choice A) Basophils are not involved in TSS. Basophilia can be seen with some myeloproliferative disorders and, rarely, certain parasitic infections.

(Choices C and E) Eosinophil activation is associated with reactions to allergens and parasites, hypersensitivity reactions to drugs, and some hematologic malignancies. Mast cells, when stimulated (due to antigen-induced cross-linking of IgE on their cell membrane), release histamine, prostaglandins, leukotrienes, and other inflammatory mediators; they are active in allergic reactions and anaphylaxis.

(Choice D) B lymphocytes respond to activation by replicating and synthesizing antibodies specific for the antigen with which they were presented; they are not responsible for TSS. Neutrophilia is commonly seen with TSS.

Educational objective:
Superantigens (eg, toxic shock syndrome toxin) interact with major histocompatibility complex molecules on antigen-presenting cells and the variable region of the T lymphocyte receptor to cause nonspecific, widespread activation of T cells. This results in the release of interleukin (IL)-2 from the T cells and IL-1 and tumor necrosis factor from macrophages. This immune cascade is responsible for the manifestations of toxic shock syndrome.

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A 24-year-old woman comes to the office due to 3 weeks of worsening throat pain and difficulty swallowing. She has no chronic medical problems but has had recurrent vulvovaginal candidiasis and bacterial folliculitis over the past year. The patient has also had an unintentional weight loss of 4.5-kg (10-lb) over the past 3 months. She is an exchange student from Senegal. Physical examination shows generalized lymphadenopathy and oropharyngeal thrush. Upper endoscopy confirms *Candida* esophagitis. HIV antigen/antibody immunoassay returns positive. Further testing shows a CD4 count of 180/mm^3 but there is no detectable plasma HIV-1 RNA. Which of the following best explains the observed laboratory findings in this patient?

A. False-positive serology from cross-reactive antibodies
B. Homozygous CCR5 deletion
C. Infection with CXCR4 tropic strain
D. Infection with HIV-2
E. Window period of HIV infection

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swallowing. She has no chronic medical problems but has had recurrent vulvovaginal candidiasis and bacterial folliculitis over the past year. The patient has also had an unintentional weight loss of 4.5-kg (10-lb) over the past 3 months. She is an exchange student from Senegal. Physical examination shows generalized lymphadenopathy and oropharyngeal thrush. Upper endoscopy confirms *Candida* esophagitis. HIV antigen/antibody immunoassay returns positive. Further testing shows a CD4 count of 180/mm^3 but there is no detectable plasma HIV-1 RNA. Which of the following best explains the observed laboratory findings in this patient?

A. False-positive serology from cross-reactive antibodies (2%)
B. Homozygous CCR5 deletion (7%)
C. Infection with CXCR4 tropic strain (7%)
✓ D. Infection with HIV-2 (59%)
E. Window period of HIV infection (23%)

Correct
59%
53 secs
01/11/2021

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Comparison of HIV-1 & HIV-2		
	HIV-1	**HIV-2**
Geographic location	Worldwide	West Africa
Viral load	High	Low
Progression to AIDS	7-10 years	10-25 years
Intrinsic resistance	Limited	NNRTIs, fusion inhibitors

NNRTIs = nonnucleoside reverse transcriptase inhibitors.

This patient's opportunistic infection (oropharyngeal/esophageal candidiasis), positive HIV immunoassay testing, and low CD4 count suggest a diagnosis of **AIDS**. However, she has no detectable HIV-1 RNA in her bloodstream. Although HIV-1 causes most cases of AIDS worldwide (and nearly all cases in the United States), AIDS can also be due to infection with **HIV-2**, which is endemic to **West Africa** (eg, Senegal).

Patients infected with HIV-2 have much **lower levels of viremia** than those infected with HIV-1. Because viremia is directly correlated with transmission risk, rate of CD4 count decline, and progression to AIDS, individuals with HIV-2 are usually less infectious and have **longer asymptomatic periods** than patients

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Patients infected with HIV-2 have much **lower levels of viremia** than those infected with HIV-1. Because viremia is directly correlated with transmission risk, rate of CD4 count decline, and progression to AIDS, individuals with HIV-2 are usually less infectious and have **longer asymptomatic periods** than patients with HIV-1. The diagnosis of HIV-2 is often suspected when **HIV test results are incongruent**; most patients will have the following laboratory results:

- **Positive fourth-generation HIV testing** (HIV antigen/antibody test) – This test evaluates for the presence of p24 antigen and HIV-1 and HIV-2 antibodies but does not usually differentiate between HIV-1 and HIV-2.
- **Indeterminate or negative HIV-1 confirmatory testing** – HIV-1 Western blot evaluates for proteins in HIV-1 and is usually indeterminate in the setting of HIV-2 infection. Plasma HIV-1 RNA testing will be negative.

Confirmation of HIV-2 infection can be made using an HIV-1/HIV-2 differentiation immunoassay. Treatment with antiretroviral therapy is required to prevent HIV-2 disease progression. However, nonnucleoside reverse transcriptase inhibitors and fusion inhibitors must be avoided because HIV-2 is intrinsically resistant to these HIV medications.

(Choice A) False-positive HIV serology can be seen in the setting of cross-reacting antibodies due to

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(Choice A) False-positive HIV serology can be seen in the setting of cross-reacting antibodies due to pregnancy, rheumatic disease, and malignancy. Although patients with cross-reacting antibodies have negative plasma HIV RNA, they would not have low CD4 counts or an AIDS-defining defining illness (eg, esophageal thrush).

(Choice B) HIV attacks host cells by binding to the host CD4 receptor and CCR5 (or CXCR4) chemokine coreceptor. Homozygous deletion to CCR5 usually prevents HIV infection because the virus is not able to enter host cells; these individuals would not typically develop low CD4 count or signs of AIDS.

(Choice C) X4 strains of HIV-1 use the chemokine receptor CXCR4 as a coreceptor during viral entry into host cells. Patients who are infected with X4 strains have positive plasma HIV-1 RNA.

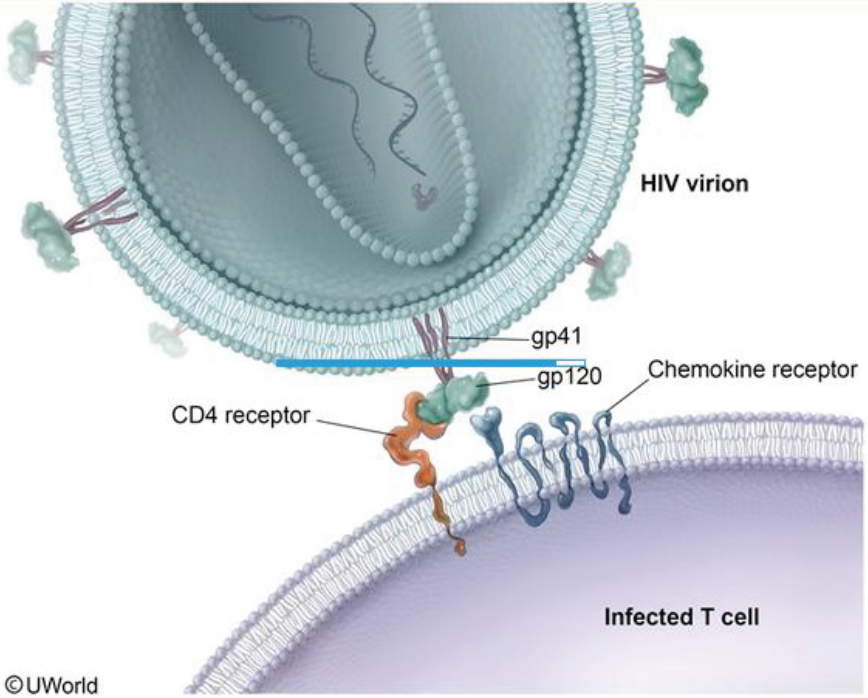
(Choice E) The window period occurs during early HIV infection when serologic testing and antigen testing for HIV are not yet positive. This patient had positive HIV antigen/antibody testing; therefore, she is not in the window period.

Educational objective:
Most cases of AIDS worldwide are caused by HIV-1. However, AIDS can also be caused by infection with HIV-2, which is endemic to West Africa. HIV-2 infection is associated with lower viral loads, less risk of transmission, and a slower progression to AIDS. The diagnosis is often suspected when HIV tests are

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enter host cells; these individuals would not typically develop low CD4 count or signs of AIDS.

(Choice C) X4 strains of HIV-1 use the chemokine receptor CXCR4 as a coreceptor during viral entry into host cells. Patients who are infected with X4 strains have positive plasma HIV-1 RNA.

(Choice E) The window period occurs during early HIV infection when serologic testing and antigen testing for HIV are not yet positive. This patient had positive HIV antigen/antibody testing; therefore, she is not in the window period.

Educational objective:

Most cases of AIDS worldwide are caused by HIV-1. However, AIDS can also be caused by infection with HIV-2, which is endemic to West Africa. HIV-2 infection is associated with lower viral loads, less risk of transmission, and a slower progression to AIDS. The diagnosis is often suspected when HIV tests are incongruent (positive screening serology but indeterminate Western blot and negative plasma HIV-1 RNA). Confirmation can be made using HIV-1/HIV-2 immunodifferentiation assay.

References

- Update on human immunodeficiency virus (HIV)-2 infection.

Microbiology Infectious Diseases HIV

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A 46-year-old woman comes to the office to be tested for HIV after one of her prior sexual partners found that he was HIV-positive. She feels healthy and has no symptoms. The patient has never had a sexually transmitted infection and has no chronic medical conditions. She has had several sexual partners in her lifetime and uses condoms inconsistently. Physical examination shows no abnormalities. HIV antigen/antibody immunoassay and a confirmatory HIV-1 antibody test are positive. Further studies reveal plasma HIV viral load is >250,000 copies/mL and CD4 lymphocyte count is 150 cells/mm^3. After discussing the results and need for treatment, the patient agrees to start antiretroviral therapy. An additional medication to prevent opportunistic infections is also planned. This added treatment is most likely being used to prevent infection from which of the following pathogens?

A. *Candida albicans*
B. *Cryptococcus neoformans*
C. Cytomegalovirus
D. *Mycobacterium avium-intracellular*
E. *Pneumocystis jirovecii*

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that he was HIV-positive. She feels healthy and has no symptoms. The patient has never had a sexually transmitted infection and has no chronic medical conditions. She has had several sexual partners in her lifetime and uses condoms inconsistently. Physical examination shows no abnormalities. HIV antigen/antibody immunoassay and a confirmatory HIV-1 antibody test are positive. Further studies reveal plasma HIV viral load is >250,000 copies/mL and CD4 lymphocyte count is 150 cells/mm^3. After discussing the results and need for treatment, the patient agrees to start antiretroviral therapy. An additional medication to prevent opportunistic infections is also planned. This added treatment is most likely being used to prevent infection from which of the following pathogens?

A. *Candida albicans*
B. *Cryptococcus neoformans*
C. Cytomegalovirus
D. *Mycobacterium avium-intracellular*
E. *Pneumocystis jirovecii*
F. *Toxoplasma gondii*

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lifetime and uses condoms inconsistently. Physical examination shows no abnormalities. HIV antigen/antibody immunoassay and a confirmatory HIV-1 antibody test are positive. Further studies reveal plasma HIV viral load is >250,000 copies/mL and CD4 lymphocyte count is 150 cells/mm^3. After discussing the results and need for treatment, the patient agrees to start antiretroviral therapy. An additional medication to prevent opportunistic infections is also planned. This added treatment is most likely being used to prevent infection from which of the following pathogens?

A. *Candida albicans* (9%)
B. *Cryptococcus neoformans* (3%)
C. Cytomegalovirus (3%)
D. *Mycobacterium avium-intracellular* (6%)
✓ E. *Pneumocystis jirovecii* (71%)
F. *Toxoplasma gondii* (6%)

Correct
71%
01 min, 29 secs
02/19/2021

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Opportunistic infections in HIV		
Infection	**Risk factors**	**Prophylaxis**
Pneumocystis jirovecii	• CD4 count <200/mm^3 • Oropharyngeal candidiasis	• Trimethoprim-sulfamethoxazole
Toxoplasma gondii	• CD4 count <100/mm^3 • Positive *Toxoplasma* IgG antibody	• Trimethoprim-sulfamethoxazole
Mycobacterium avium complex (*M avium* & *M intracellulare*)	• CD4 count <50/mm^3	• Azithromycin

Patients with **HIV** have progressive impairment of the cell-mediated immune response that puts them at risk for **opportunistic infections** (OIs) with bacterial, viral, fungal, and protozoal pathogens. OIs are associated with significant morbidity and mortality and also worsen HIV progression and viremia. **Antimicrobial prophylaxis** can decrease the risk of developing certain OIs and is recommended in addition to antiretroviral therapy for all patients with HIV who have CD4 counts <200/mm^3

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addition to antiretroviral therapy for all patients with HIV who have CD4 counts **<200/mm³**.

Antimicrobial prophylaxis is guided by the patient's CD4 count, as follows:

- CD4 count <200/mm³ – Antimicrobial prophylaxis against ***Pneumocystis jiroveci* pneumonia** is indicated. **Trimethoprim-sulfamethoxazole** is the first-line agent.
- CD4 count <100/mm³ – Patients require antimicrobial prophylaxis against *Toxoplasma gondii* reactivation if they have serologic evidence of previous exposure (positive *Toxoplasma* IgG antibody). Trimethoprim-sulfamethoxazole is also used for prophylaxis against this condition **(Choice F)**.
- CD4 count <50/mm³ – Patients require antimicrobial prophylaxis against *Mycobacterium avium-intracellular* (mycobacterium avium complex). Azithromycin is used most commonly **(Choice D)**.

Once CD4 counts improve with antiretroviral therapy (>200/mm³ for >3 months), patients can often stop taking antimicrobial prophylaxis.

(Choice A) Patients with advanced HIV who have low CD4 counts are at greater risk for mucocutaneous *Candida* infections (eg, thrush, esophagitis). However, routine prophylaxis against *Candida* infection is not recommended due to risk of drug resistance and drug interactions.

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recommended due to risk of drug resistance and drug interactions.

(Choice B) Patients with HIV who have CD4 counts <100/mm^3 are at risk for cryptococcal meningitis. However, prophylaxis is not recommended against *Cryptococcus* due to drug interactions, adverse effects, risk of fungal resistance, and cost. This patient's CD4 count >100/mm^3.

(Choice C) Cytomegalovirus (CMV) is a common OI in patients with HIV who have CD4 counts <50/mm^3. Reactivation frequently leads to retinitis and gastrointestinal disease (eg, colitis). However, primary prophylaxis against CMV is not recommended due to cost, toxicity, and the high number needed to treat to reduce risk of disease.

Educational objective:
Patients with advanced HIV and low CD4 counts are at risk for opportunistic infections and require antimicrobial prophylaxis. *Pneumocystis jiroveci* pneumonia prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) is indicated when CD4 count is <200/mm^3.

Microbiology	Infectious Diseases	HIV
Subject	System	Topic

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A 12-year-old boy is brought to the emergency department due to a skin infection. Temperature is 38.4 C (101.1 F). Physical examination shows an area of erythema, warmth, and tenderness on his right distal leg. Laboratory results are notable for leukocytosis. The patient is started on intravenous nafcillin. Two days later, he shows limited response to antibiotic therapy. Light microscopy of pus obtained from the site shows gram-positive cocci in clusters, and sensitivity testing demonstrates little response to nafcillin but good response to vancomycin. Which of the following is the most likely explanation for nafcillin treatment failure in this patient?

A. Active drug transport out of the cell
B. Enzymatic degradation of the drug
C. Mutation in DNA gyrase
D. Mutation in RNA polymerase
E. Poor interaction with binding proteins

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A 12-year-old boy is brought to the emergency department due to a skin infection. Temperature is 38.4 C (101.1 F). Physical examination shows an area of erythema, warmth, and tenderness on his right distal leg. Laboratory results are notable for leukocytosis. The patient is started on intravenous nafcillin. Two days later, he shows limited response to antibiotic therapy. Light microscopy of pus obtained from the site shows gram-positive cocci in clusters, and sensitivity testing demonstrates little response to nafcillin but good response to vancomycin. Which of the following is the most likely explanation for nafcillin treatment failure in this patient?

A. ~~Active drug transport out of the cell~~ (3%)
B. Enzymatic degradation of the drug (20%)
C. ~~Mutation in DNA gyrase~~ (1%)
D. ~~Mutation in RNA polymerase~~ (1%)
E. Poor interaction with binding proteins (73%)

73% 01 min 41 secs 02/23/2021

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Penicillins	• Beta-lactamase, ESBL • Mutated PBP • Mutated porin protein
Vancomycin	• Mutated peptidoglycan cell wall • Impaired influx/increased efflux
Quinolones	• Mutated DNA gyrase • Impaired influx/increased efflux
Aminoglycosides	• Aminoglycoside-modifying enzymes • Mutated ribosomal subunit protein • Mutated porin protein
Tetracyclines	• Impaired influx/increased efflux • Inactivated enzyme
Rifamycins	• Mutated RNA polymerase

ESBL = extended-spectrum beta-lactamase; **PBP** = penicillin-binding protein.

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The presence of gram-positive cocci in clusters that do not respond to nafcillin but show sensitivity to vancomycin suggests infection with **methicillin-resistant *Staphylococcus aureus*** (MRSA). *S aureus* is a common cause of skin infections in the United States. Most skin infections are minor, but *S aureus* can cause serious infections (eg, surgical wound infections, bloodstream infections in the presence of central intravenous catheters, pneumonia).

S aureus strains that are resistant to oxacillin, nafcillin, and methicillin have been historically termed **MRSA**, but they are also resistant to all β-lactam agents, including penicillin, cephalosporins (except ceftaroline, a fifth-generation cephalosporin), and carbapenems. Methicillin (nafcillin) **resistance** is typically mediated by alterations in the structure of **penicillin-binding proteins** (PBP), the enzymes involved in cell wall synthesis. Altered PBPs, especially PBP2a, have greatly **reduced affinity** for β-lactam antimicrobial agents (except ceftaroline).

(Choice A) Resistance to tetracycline and sulfonamides is due at least in part to a decrease in the levels of drug accumulation due to decreased uptake and/or increased efflux.

(Choice B) Approximately 95% of *S aureus* isolates in the United States produce penicillinase, which causes penicillin resistance by breaking penicillin's β-lactam ring. However, nafcillin is penicillinase-stable (along with oxacillin and methicillin)

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agents (except ceftaroline).

(Choice A) Resistance to tetracycline and sulfonamides is due at least in part to a decrease in the levels of drug accumulation due to decreased uptake and/or increased efflux.

(Choice B) Approximately 95% of *S aureus* isolates in the United States produce penicillinase, which causes penicillin resistance by breaking penicillin's β-lactam ring. However, nafcillin is penicillinase-stable (along with oxacillin and methicillin).

(Choices C and D) Mutations in DNA gyrase cause resistance to quinolone antibiotics. Mutations in RNA polymerase cause resistance to rifampin.

Educational objective:
Methicillin-resistant *Staphylococcus aureus* is resistant to all β-lactam antibiotics, including beta-lactamase-resistant antibiotics, as it has an altered penicillin-binding protein that does not bind β-lactams effectively.

Pharmacology	Infectious Diseases	Antibiotic resistance
Subject	System	Topic

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A 34-year-old man came to the office due to white plaques on his buccal mucosa that he incidentally discovered while brushing his teeth. After appropriate workup, he was found to be HIV positive, with a CD4+ T lymphocyte count of 280/mm^3. He was referred to an infectious diseases specialist for follow-up but was noncompliant with appointments. The patient returns 3 years later due to several months of pain and itching in the perirectal area. He also has intermittent rectal bleeding and often sees bright red blood on the tissue after wiping. The patient did not seek medical care because he thought he had hemorrhoids. On examination, a single, hard mass with superficial ulceration measuring approximately 2x2 cm is noted in the anal canal. No hemorrhoids are present. There is no palpable regional lymphadenopathy. Which of the following pathogens is most likely responsible for this patient's current anal pathology?

A. Adenovirus
B. *Candida albicans*
C. *Chlamydia trachomatis*
D. Cytomegalovirus
E. Epstein-Barr virus

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and itching in the perirectal area. He also has intermittent rectal bleeding and often sees bright red blood on the tissue after wiping. The patient did not seek medical care because he thought he had hemorrhoids. On examination, a single, hard mass with superficial ulceration measuring approximately 2x2 cm is noted in the anal canal. No hemorrhoids are present. There is no palpable regional lymphadenopathy. Which of the following pathogens is most likely responsible for this patient's current anal pathology?

- A. Adenovirus
- B. *Candida albicans*
- C. *Chlamydia trachomatis*
- D. Cytomegalovirus
- E. Epstein-Barr virus
- F. Herpes simplex virus type 2
- G. Human papillomavirus

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and itching in the perirectal area. He also has intermittent rectal bleeding and often sees bright red blood on the tissue after wiping. The patient did not seek medical care because he thought he had hemorrhoids. On examination, a single, hard mass with superficial ulceration measuring approximately 2x2 cm is noted in the anal canal. No hemorrhoids are present. There is no palpable regional lymphadenopathy. Which of the following pathogens is most likely responsible for this patient's current anal pathology?

- A. ~~Adenovirus~~ (0%)
- B. ~~*Candida albicans*~~ (5%)
- C. ~~*Chlamydia trachomatis*~~ (2%)
- D. Cytomegalovirus (7%)
- E. Epstein-Barr virus (4%)
- F. Herpes simplex virus type 2 (10%)
- ✓ G. Human papillomavirus (67%)

Correct

67%
Answered correctly

01 min, 07 secs
Time Spent

11/02/2020
Last Updated

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This patient with HIV likely has **anal squamous cell carcinoma** given the duration of pain, itching, and rectal bleeding in addition to the visible **ulcerative mass** (anal cancers are ulcerative in >50% of cases). Anogenital squamous cell carcinomas and their precursors, squamous intraepithelial lesions, have been linked to **human papillomavirus** (HPV) infection. Intraepithelial neoplasias of the cervix, vulva, penis, and anus have a well-documented association with HPV types 16 and 18. A strong correlation between HPV and invasive carcinoma has been established for cervical cancer.

Immunodeficiency states (eg, AIDS) increase host susceptibility to HPV infection and more severe infection. **HIV**-positive men who have sex with men are at increased risk of developing anal squamous cell carcinoma (anal intercourse is hypothesized to be related), and HIV-positive women are more prone to developing cervical squamous cell carcinoma.

(Choice A) Adenoviruses can cause severe upper respiratory illnesses, pneumonia, and disseminated infection in immunosuppressed patients.

(Choices B and E) HIV-positive patients often experience reactivation of latent Epstein-Barr virus (EBV) infection. EBV replication in such patients is associated with certain lymphomas and with oral hairy leukoplakia, which typically manifests as white plaques on the lateral tongue margins (this patient's white buccal plaques on initial diagnosis were more likely thrush due to *Candida*).

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buccal plaques on initial diagnosis were more likely thrush due to *Candida*).

(Choice C) *Chlamydia trachomatis* causes lymphogranuloma venereum (LGV), characterized by an ulcerative or vesicular lesion on the external genitalia followed by significant regional lymphadenopathy. Proctitis with tenesmus and bloody discharge can be seen with both LGV and anal carcinoma; however, LGV has a less indolent clinical course, and painful lymphadenopathy is a cardinal feature.

(Choice D) HIV-positive patients with CD4+ cell counts <100/mm^3 are at significantly increased risk of developing cytomegalovirus (CMV) infection, which most frequently causes retinitis in AIDS patients. CMV involvement of the gastrointestinal tract typically manifests as esophageal ulcers or colitis, not anal masses.

(Choice F) Although AIDS increases the prevalence of herpes simplex virus type 2 (HSV-2) infection and the frequency of symptomatic genital herpes recurrences, HSV-2 is not typically associated with anogenital carcinoma. A large, hard mass is not characteristic of herpetic lesions (classically painful vesicles or ulcers).

Educational objective:
Human papillomavirus (HPV) types 16 and 18 are strongly associated with anal and cervical squamous cell carcinoma. HIV infection increases the prevalence of HPV infection and the risk of anal carcinoma; this

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LGV has a less indolent clinical course, and painful lymphadenopathy is a cardinal feature.

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Educational objective:
Human papillomavirus (HPV) types 16 and 18 are strongly associated with anal and cervical squamous cell carcinoma. HIV infection increases the prevalence of HPV infection and the risk of anal carcinoma; this risk is further augmented in men who have sex with men.

References

- Risk of human papillomavirus-associated cancers among persons with AIDS.
- Anal cancer: an overview

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www.ncbi.nlm.nih.gov/pubmed/19648510

The antiviral activity of a guanosine derivative is tested by examining cells infected with different viruses for characteristic abnormal changes in cell morphology due to the viruses. These changes are known as the cytopathic effect (CPE). In the presence of significant antiviral activity, CPE will be inhibited. The following results are obtained from the study:

	CPE without antiviral agent	CPE with antiviral agent
Herpes simplex virus 1	+++	–
Herpes simplex virus 2	+++	–
Epstein-Barr virus	+++	++
Varicella zoster virus	+++	–
Cytomegalovirus	+++	++

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Epstein-Barr virus	+++	++
Varicella zoster virus	+++	–
Cytomegalovirus	+++	++

A difference in which of the following best explains the variation in susceptibility of the various viruses to this specific antiviral agent?

A. DNA polymerase structure
B. Drug degradation rate
C. Drug phosphorylation rate
D. Viral capsid protein composition
E. Viral protease activity

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Epstein-Barr virus	+++	++
Varicella zoster virus	+++	–
Cytomegalovirus	+++	++

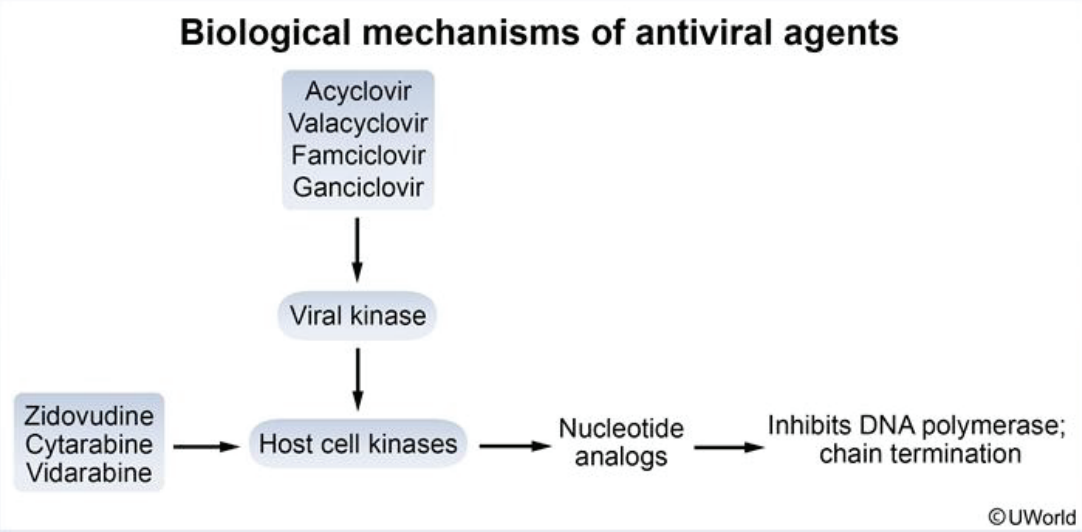
A difference in which of the following best explains the variation in susceptibility of the various viruses to this specific antiviral agent?

A. DNA polymerase structure (23%)
B. ~~Drug degradation rate~~ (1%)
C. Drug phosphorylation rate (43%)
D. ~~Viral capsid protein composition~~ (19%)
E. ~~Viral protease activity~~ (11%)

43%
02 mins, 23 secs
12/22/2020

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www.ncbi.nlm.nih.gov/pubmed/19648510



The drug described in this study demonstrates significant antiviral activity (cytopathic effect) against herpes simplex virus type 1 (HSV 1), HSV 2, and varicella zoster virus (VZV) but has weak activity against Epstein-Barr virus (EBV) and cytomegalovirus (CMV). This agent is most likely **acyclovir**, a guanosine analog. Once acyclovir enters the HSV-infected host cell, it is **phosphorylated** to acyclovir monophosphate, principally via a **virally**-encoded thymidine kinase (TK). This is the **rate-limiting** step in acyclovir

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activation. Acyclovir monophosphate is then phosphorylated by **cellular** enzymes into the active triphosphate form, which impairs viral DNA polymerase-mediated replication of HSV.

EBV and CMV do not produce the same TK as HSV and VZV. As a result, EBV- or CMV-infected cells cannot easily convert acyclovir into its pharmacologically active form. At very high intracellular concentrations of acyclovir, some of the drug appears to be activated by unidentified cellular phosphorylating enzymes, which may explain the partial susceptibility of EBV and CMV to higher acyclovir doses. The partial activity of acyclovir against CMV may also be mediated by inhibited synthesis of a virus-specific polypeptide.

(Choices A, B, and E) Mutations in viral DNA polymerase can lead to acyclovir resistance, but differences in TK are the best explanation for the observed results. Drug degradation rate and viral protease activity are not responsible for differences in viral susceptibility to acyclovir.

(Choice D) TK is an enzyme produced in infected cells, but it is not present in the capsid.

Educational objective:
Monophosphorylation of acyclovir by a viral thymidine kinase is the first (and rate-limiting) step in conversion of acyclovir to its active triphosphate form. Acyclovir and related drugs (eg, famciclovir, valacyclovir) are more effective against herpes simplex virus and varicella-zoster virus than cytomegalovirus

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www.ncbi.nlm.nih.gov/pubmed/19648510

cannot easily convert acyclovir into its pharmacologically active form. At very high intracellular concentrations of acyclovir, some of the drug appears to be activated by unidentified cellular phosphorylating enzymes, which may explain the partial susceptibility of EBV and CMV to higher acyclovir doses. The partial activity of acyclovir against CMV may also be mediated by inhibited synthesis of a virus-specific polypeptide.

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(Choice D) TK is an enzyme produced in infected cells, but it is not present in the capsid.

Educational objective:
Monophosphorylation of acyclovir by a viral thymidine kinase is the first (and rate-limiting) step in conversion of acyclovir to its active triphosphate form. Acyclovir and related drugs (eg, famciclovir, valaciclovir) are more effective against herpes simplex virus and varicella zoster virus than cytomegalovirus and Epstein-Barr virus.

Pharmacology	Infectious Diseases	Acyclovir
Subject	System	Topic

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www.ncbi.nlm.nih.gov/pubmed/19648510

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A 34-year-old woman comes to the emergency department due to 6 days of fatigue and intermittent fever. Medical history is significant for depression. She does not use tobacco, alcohol, or illicit drugs and has no drug allergies. The patient lives in New York City and recently traveled to central Africa, where she helped establish a nutrition program. Her blood microscopy findings are shown in the exhibit. Urine pregnancy test is negative. Which of the following is the best treatment for this patient?

A. Atovaquone and proguanil
B. Ceftriaxone and doxycycline
C. Chloroquine and primaquine
D. Metronidazole and paromomycin
E. Trimethoprim and sulfamethoxazole

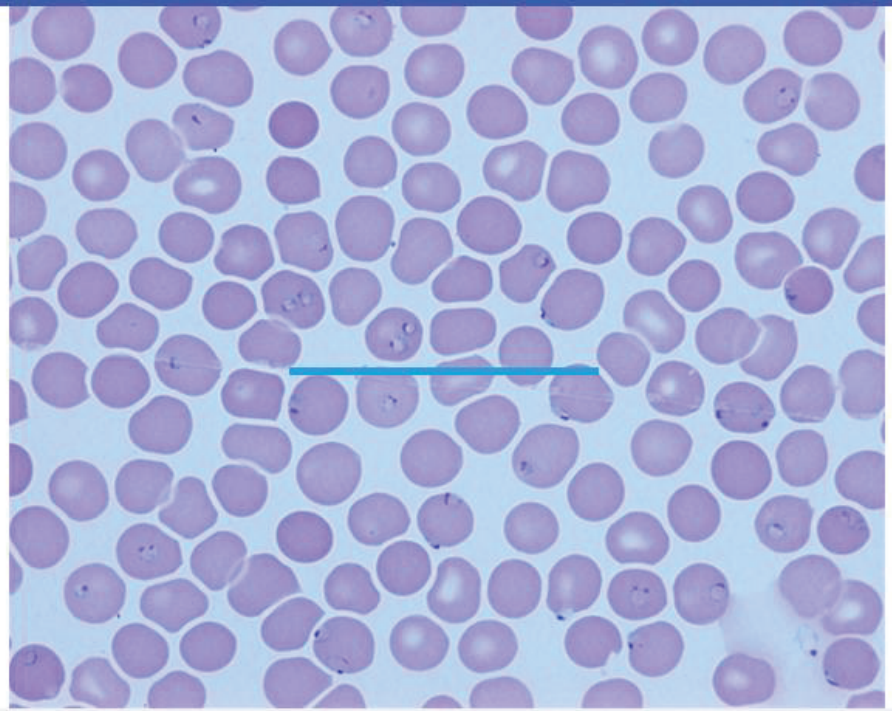
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Exhibit Display



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A 34-year-old woman comes to the emergency department due to 6 days of fatigue and intermittent fever. Medical history is significant for depression. She does not use tobacco, alcohol, or illicit drugs and has no drug allergies. The patient lives in New York City and recently traveled to central Africa, where she helped establish a nutrition program. Her blood microscopy findings are shown in the exhibit. Urine pregnancy test is negative. Which of the following is the best treatment for this patient?

- A. Atovaquone and proguanil (27%)
- B. ~~Ceftriaxone and doxycycline~~ (1%)
- C. Chloroquine and primaquine (68%)
- D. ~~Metronidazole and paromomycin~~ (1%)
- E. ~~Trimethoprim and sulfamethoxazole~~ (1%)

Correct

27%
Answered correctly

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Last Updated

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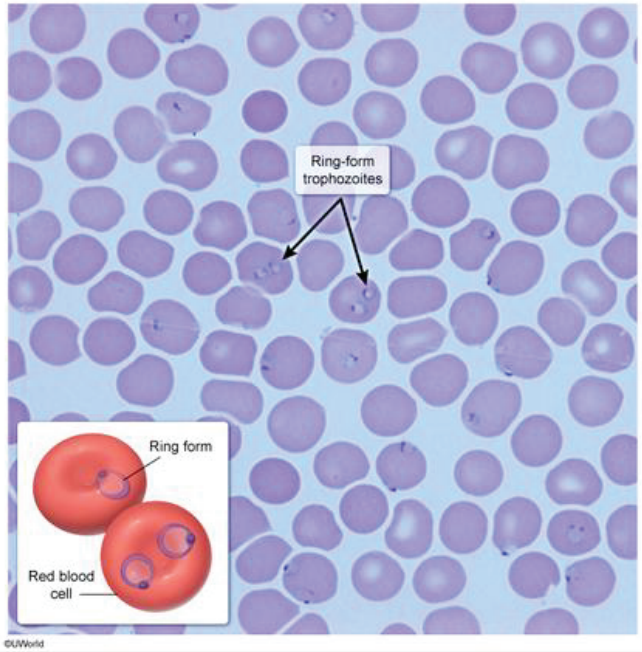
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Plasmodium falciparum

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Plasmodium falciparum



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Although fever and fatigue are nonspecific symptoms, this patient's peripheral blood smear is diagnostic of **malaria**, a disease endemic to Africa and Latin America that is caused by 4 main species of ***Plasmodium***. The diagnosis is frequently made by examination of a peripheral blood smear with Giemsa staining. In *Plasmodium falciparum* infection, red blood cells have multiple **small rings** representing developing **trophozoites** (arrows) and banana-shaped gametocytes (not shown).

For malaria acquired in areas known to have chloroquine-sensitive organisms, chloroquine is the treatment of choice. Many African species are **chloroquine-resistant**; these can be treated with **atovaquone-proguanil** or **artemisinins**, which are well tolerated and have excellent cure rates. *P vivax* and *P ovale* have dormant liver forms (hypnozoites) that require the addition of primaquine therapy.

(Choice B) Early disseminated Lyme disease is associated with neurologic (eg, facial nerve palsy) and cardiac (eg, atrioventricular block, carditis) manifestations and is often treated with ceftriaxone. *Ixodes scapularis*, the tick that transmits Lyme disease, can also transmit babesiosis and ehrlichiosis, which can be treated with doxycycline. Although *Babesia* can appear as ring-like structures within blood cells, it is differentiated by the presence of 4 rings arranged in a Maltese cross pattern, which is pathognomonic for the disease.

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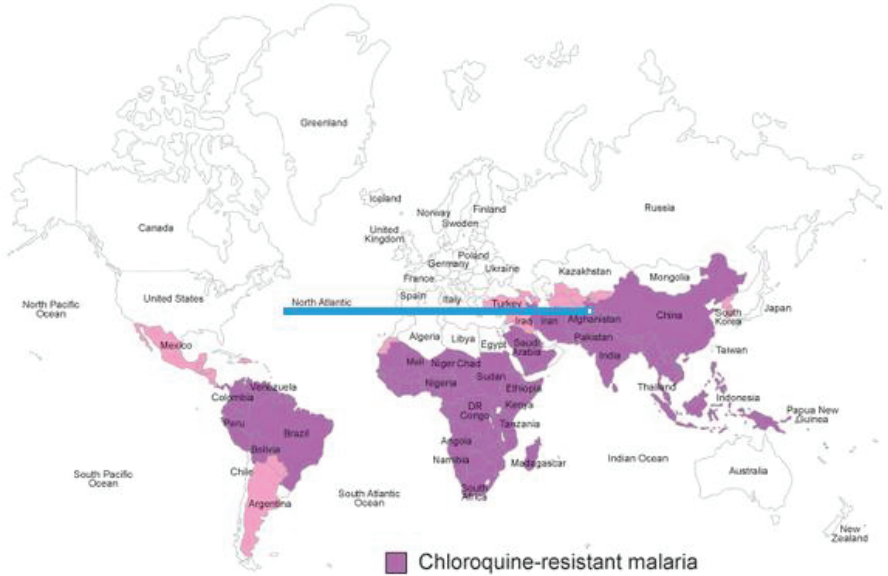
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Map of malaria regions



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Babesia



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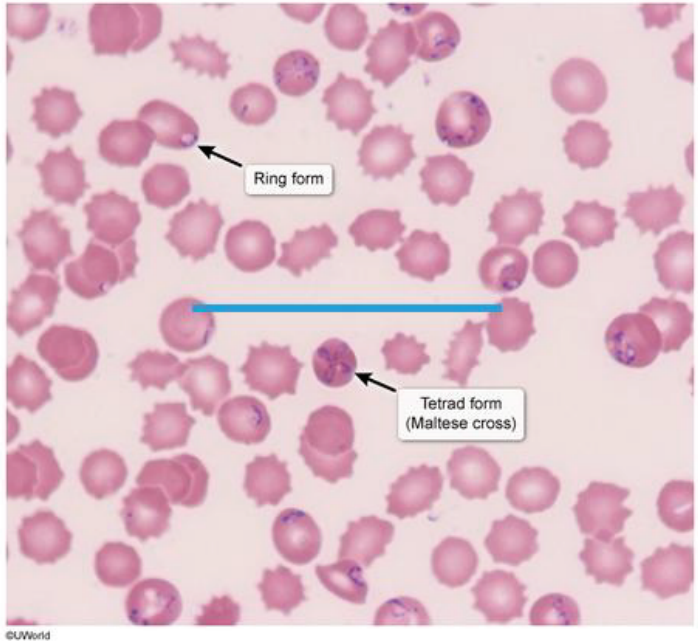
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Exhibit Display

Babesia



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the disease.

(Choice C) *P falciparum* is the predominant malaria strain in Africa. Most *P falciparum* in Africa are resistant to chloroquine, so alternate agents (eg, atovaquone-proguanil, artemisinins) are required for treatment. Because *P falciparum* does not have a dormant hepatic phase, primaquine is not required.

(Choice D) *Entamoeba histolytica* is an amebic parasite that can cause dysentery (bloody diarrhea) and extraintestinal abscess in the liver (most common), lung, or brain. It is typically treated with metronidazole, to kill the trophozoites, and paromomycin, to eliminate residual cysts in the gastrointestinal lumen.

(Choice E) Trimethoprim-sulfamethoxazole is used to treat *Pneumocystis* pneumonia, which is most common in individuals with untreated AIDS or those taking chronic steroids. Patients usually present with slowly worsening dyspnea, dry cough, hypoxia, and diffuse interstitial infiltrates.

Educational objective:

Red blood cells filled with multiple, small rings suggest *Plasmodium* infection (malaria). Erythrocytic forms of this parasite may be treated with antimalarials such as chloroquine (in non-resistant areas), atovaquone-proguanil, and artemisinins. Primaquine is required to kill *P vivax* and *P ovale* liver hypnozoites.

References

- Guidelines for the Treatment of Malaria.

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A 29-year-old woman comes to the office with malaise, fever, and extremely painful genital lesions. She has never had such symptoms before. She is sexually active with a new partner. On examination, the patient has several tiny, thin-walled vesicles on an erythematous base and exquisitely tender, shallow ulcers on the labia. Tender inguinal lymphadenopathy is present. Tzanck smear of the genital lesions shows multinucleated giant cells. A drug is prescribed that can be used to manage this acute episode and prevent future episodes of this patient's condition. This drug most likely works by which of the following mechanisms?

A. Incorporation into newly replicating viral DNA
B. Inhibition of viral protease activity
C. Inhibition of virion release from infected cells
D. Prevention of viral entry into the target cells
E. Upregulation of interferon synthesis in infected cells

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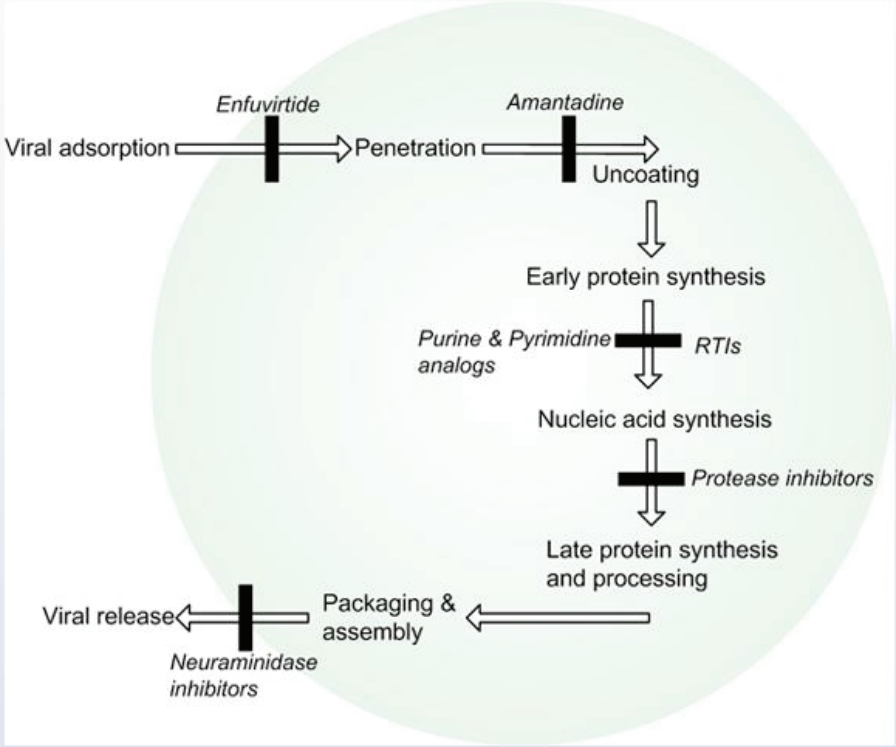
A 29-year-old woman comes to the office with malaise, fever, and extremely painful genital lesions. She has never had such symptoms before. She is sexually active with a new partner. On examination, the patient has several tiny, thin-walled vesicles on an erythematous base and exquisitely tender, shallow ulcers on the labia. Tender inguinal lymphadenopathy is present. Tzanck smear of the genital lesions shows multinucleated giant cells. A drug is prescribed that can be used to manage this acute episode and prevent future episodes of this patient's condition. This drug most likely works by which of the following mechanisms?

- A. Incorporation into newly replicating viral DNA (69%)
- B. Inhibition of viral protease activity (13%)
- C. Inhibition of virion release from infected cells (8%)
- D. Prevention of viral entry into the target cells (6%)
- E. Upregulation of interferon synthesis in infected cells (2%)

60% 59 secs 02/04/2021

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This patient's new genital rash and positive Tzanck smear are consistent with a **primary genital herpes**

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This patient's new genital rash and positive Tzanck smear are consistent with a **primary genital herpes** simplex virus (HSV) infection, likely due to HSV-2. **Antiviral drugs** for the treatment of primary genital herpes include acyclovir, valacyclovir (acyclovir prodrug with better oral bioavailability), and famciclovir. Acyclovir treatment during a primary episode can reduce duration of viral shedding, time to lesional healing, constitutional symptoms, and local pain. Chronic daily suppressive therapy (lower dose) can be used in patients who have recurrent episodes.

In infected host cells, acyclovir (a **nucleoside analog**) is converted into acyclovir monophosphate principally via **virus-encoded** thymidine kinase. Cellular enzymes then convert the monophosphate into acyclovir triphosphate, which competes with deoxyguanosine triphosphate for viral DNA polymerase. When acyclovir triphosphate becomes incorporated into the replicating viral DNA chain, viral DNA synthesis is terminated.

Acyclovir does not significantly impact uninfected cells in vitro as uptake into these cells is poor, phosphorylation in the absence of viral thymidine kinase is minimal, and cellular α-DNA polymerase has significantly less affinity for acyclovir triphosphate than does viral DNA polymerase.

(Choice B) Inhibition of viral protease activity is the mechanism of action for drugs such as indinavir, an antiretroviral used in HIV treatment.

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antiretroviral used in HIV treatment.

(Choice C) Prevention of virion release from infected cells is the mechanism of action for drugs such as neuraminidase inhibitors (eg, oseltamivir), which are used in the early treatment of influenza.

(Choice D) Drugs such as enfuvirtide and maraviroc, antiretrovirals used in HIV treatment, prevent viral entry into the target cells. Docosanol, a topical agent that prevents viral entry, is sometimes used for herpes labialis, not genital HSV.

(Choice E) Upregulation of interferon synthesis in infected cells is accomplished by many interleukins.

Educational objective:
Antiviral drugs currently recommended for the treatment of primary genital herpes include the nucleoside analogs (eg, acyclovir). These are incorporated into newly replicating viral DNA and ultimately terminate viral DNA chain synthesis.

Pharmacology	Infectious Diseases	Acyclovir
Subject	System	Topic

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An outbreak of diarrheal illness occurs in a community after a massive hurricane. The affected patients experience voluminous, watery diarrhea that quickly leads to severe dehydration. Stool examinations of these patients yield oxidase-positive, curved, highly motile, gram-negative rods. Epidemiologic study reveals the source as a contaminated water supply. Which of the following patient populations would be most susceptible to developing this illness?

A. Patients lacking a functional spleen
B. Patients taking proton pump inhibitors
C. Patients who recently took antibiotics
D. Patients with chronic liver disease
E. Patients with cystic fibrosis

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An outbreak of diarrheal illness occurs in a community after a massive hurricane. The affected patients experience voluminous, watery diarrhea that quickly leads to severe dehydration. Stool examinations of these patients yield oxidase-positive, curved, highly motile, gram-negative rods. Epidemiologic study reveals the source as a contaminated water supply. Which of the following patient populations would be most susceptible to developing this illness?

A. ~~Patients lacking a functional spleen~~ (8%)
B. Patients taking proton pump inhibitors (65%)
C. Patients who recently took antibiotics (9%)
D. Patients with chronic liver disease (3%)
E. Patients with cystic fibrosis (12%)

Correct

65% Answered correctly

48 secs Time Spent

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Vibrio cholerae is a comma-shaped, oxidase-positive, highly motile, gram-negative rod that is acquired after ingesting contaminated food or water. The infection is not invasive and does not disseminate outside of the gastrointestinal tract. However, the elaboration of the cholera enterotoxin leads to **severe, watery diarrhea** that can cause death from electrolyte imbalance and dehydration within 12 hours of symptom onset. Cholera is endemic in southern Asia and parts of Africa and Latin America, where seasonal outbreaks are common (peaks occur prior to and after rainy seasons). In the United States, the disease is rare and occurs mainly in patients who ingest contaminated seafood from the Gulf Coast.

V cholerae must survive the acidic environment of the stomach to reach the small intestine and cause disease. Because the organism is very **acid-sensitive**, a high burden of *V cholerae* is generally required to cause clinical symptoms (>10^{10} organisms from contaminated water or >10^{8} organisms from contaminated food). However, those with inadequate gastric acid production (**achlorhydria**) can develop the disease with **much smaller infectious doses** as there is insufficient acid to kill the bacteria. Patients on long-term **proton pump inhibitor therapy** (eg, omeprazole) have pharmacologically induced achlorhydria; it can also be seen in those with gastritis.

(Choice A) Patients with splenectomy are at much higher risk of fulminant infection with encapsulated bacteria such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*. *V*

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achlorhydria; it can also be seen in those with gastritis.

(Choice A) Patients with splenectomy are at much higher risk of fulminant infection with encapsulated bacteria such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*. *V cholerae* is not encapsulated and not invasive; patients with splenectomy are unlikely to be at greater risk.

(Choice C) Recent antibiotic use is a strong risk factor for *Clostridium difficile* colitis, which typically manifests with watery diarrhea, abdominal pain, and low-grade fever. *C difficile* is a spore-forming, toxin-producing, gram-positive organism.

(Choice D) Patients with chronic liver disease are at increased risk for severe disease with *Vibrio vulnificus*, which can cause watery diarrhea. However, the ingestion of this pathogen usually leads to severe, rapid-onset sepsis in susceptible patients. In addition, *V vulnificus* is more likely to cause wound infections than gastroenteritis.

(Choice E) Patients with cystic fibrosis are at high risk for infections with *Pseudomonas aeruginosa*, an oxidase-positive, gram-negative rod. This pathogen is a common cause of pneumonia in this population; it does not cause gastroenteritis outbreaks.

Educational objective:

Vibrio cholerae must survive the acidic environment of the stomach to reach the small intestine and cause

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producing, gram-positive organism.

(Choice D) Patients with chronic liver disease are at increased risk for severe disease with *Vibrio vulnificus*, which can cause watery diarrhea. However, the ingestion of this pathogen usually leads to severe, rapid-onset sepsis in susceptible patients. In addition, *V vulnificus* is more likely to cause wound infections than gastroenteritis.

(Choice E) Patients with cystic fibrosis are at high risk for infections with *Pseudomonas aeruginosa*, an oxidase-positive, gram-negative rod. This pathogen is a common cause of pneumonia in this population; it does not cause gastroenteritis outbreaks.

Educational objective:

Vibrio cholerae must survive the acidic environment of the stomach to reach the small intestine and cause disease. Because the organism is easily destroyed by acid, a high burden of organisms must be ingested to cause infection. However, conditions that decrease gastric acidity (eg, antacid use) lower the minimum infectious dose of *V cholerae* by multiple orders of magnitude.

References

- Cholera.

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A 23-year-old man comes to the office due to several days of dysuria. He has had no fever or hematuria. The patient has no other medical conditions, takes no medications, and has no known allergies. Temperature is 37.1 C (98.8 F). On genitourinary examination, mucopurulent discharge is noted at the urethral meatus. Microscopy of the discharge shows numerous neutrophils, some of which contain intracellular gram-negative diplococci. A single intramuscular injection of ceftriaxone is administered. Which of the following additional medications is recommended at this time?

A. Doxycycline
B. Fluconazole
C. Metronidazole
D. No additional medication
E. Penicillin G benzathine
F. Trimethoprim-sulfamethoxazole

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A 23-year-old man comes to the office due to several days of dysuria. He has had no fever or hematuria. The patient has no other medical conditions, takes no medications, and has no known allergies. Temperature is 37.1 C (98.8 F). On genitourinary examination, mucopurulent discharge is noted at the urethral meatus. Microscopy of the discharge shows numerous neutrophils, some of which contain intracellular gram-negative diplococci. A single intramuscular injection of ceftriaxone is administered. Which of the following additional medications is recommended at this time?

- A. Doxycycline (89%) ✓
- B. Fluconazole (0%)
- C. Metronidazole (1%)
- D. No additional medication (4%) ✗
- E. ~~Penicillin G benzathine~~ (1%)
- F. ~~Trimethoprim-sulfamethoxazole~~ (1%)

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Infectious urethritis in men	
Etiology	• *Neisseria gonorrhoeae* • *Chlamydia trachomatis* • *Mycoplasma genitalium* • *Trichomonas vaginalis*
Manifestations	• Dysuria • Discharge
Diagnosis	• Gram stain & culture • Nucleic acid amplification testing
Treatment	• GU alone: ceftriaxone • GU + *Chlamydia**: ceftriaxone + doxycycline • *Chlamydia*/*Mycoplasma*: azithromycin • *Trichomonas*: metronidazole

*GU + uncertain *Chlamydia* status is also treated with

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*GU + uncertain *Chlamydia* status is also treated with ceftriaxone + doxycycline.

GU = gonococcal urethritis.

This young man with dysuria and penile discharge likely has **infectious urethritis** due to sexually transmitted infection. Most cases are caused by *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or *Mycoplasma genitalium*; **simultaneous infection** with multiple pathogens is common.

Nucleic acid amplification testing (NAAT) of urethral, vaginal, or anal swabs is used to identify the causative organism. When available, light microscopy with **Gram stain** is performed to rapidly diagnose *N gonorrhoeae* infection while awaiting NAAT results. **Gonococcal urethritis** is diagnosed when there are leukocytes with **intracellular gram-negative diplococci**; nongonococcal urethritis is diagnosed when there are no organisms present (because *C trachomatis* does not have significant peptidoglycan in the cell wall, it cannot be identified on Gram stain).

Treatment is as follows:

- **Gonorrhea with positive/uncertain *Chlamydia* status** (as in this patient) is treated with **ceftriaxone and doxycycline** to provide dual coverage for gonorrhea (ceftriaxone plus doxycycline) and coverage for potential *Chlamydia* coinfection (doxycycline).

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- **Gonorrhea with positive/uncertain *Chlamydia* status** (as in this patient) is treated with **ceftriaxone and doxycycline** to provide dual coverage for gonorrhea (ceftriaxone plus doxycycline) and coverage for potential *Chlamydia* coinfection (doxycycline).
- Gonorrhea with negative Chlamydia NAAT is treated with ceftriaxone alone **(Choice D)**.
- Positive *Chlamydia* with no gonorrhea is treated with azithromycin or doxycycline monotherapy.

(Choice B) Fluconazole is a triazole-class antifungal agent used to treat candidiasis, cryptococcosis, histoplasmosis, blastomycosis, and coccidioidomycosis. Fungal urethritis is uncommon in otherwise healthy men.

(Choice C) Metronidazole is treats anaerobic bacteria and protozoa. It has no activity against *N gonorrhoeae* or *C trachomatis* but can be used for urethritis caused by *Trichomonas vaginalis*. Because *T vaginalis* is a less common cause of infectious urethritis in men, empiric coverage against *T vaginalis* is not recommended.

(Choice E) Penicillin G benzathine is used to treat syphilis infection, which typically presents with a chancre (primary syphilis) or diffuse rash and lymphadenopathy (secondary syphilis). Treatment for syphilis is not indicated without these characteristic symptoms or a positive syphilis test result.

(Choice F) Trimethoprim-sulfamethoxazole is used to treat cystitis or proctitis due to coliform bacilli (eg,

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vaginalis is a less common cause of infectious urethritis in men, empiric coverage against *T vaginalis* is not recommended.

(Choice E) Penicillin G benzathine is used to treat syphilis infection, which typically presents with a chancre (primary syphilis) or diffuse rash and lymphadenopathy (secondary syphilis). Treatment for syphilis is not indicated without these characteristic symptoms or a positive syphilis test result.

(Choice F) Trimethoprim-sulfamethoxazole is used to treat cystitis or proctitis due to coliform bacilli (eg, *Escherichia coli*). These organisms can cause urethritis in older men in the setting of prostatic obstruction of the urethra. However, infectious urethritis in young men is almost always caused by sexually transmitted infection, not coliform organisms.

Educational objective:
Urethritis in young men is usually due to sexually transmitted infection. Treatment for gonococcal urethritis with uncertain or positive *Chlamydia* coinfection status is ceftriaxone plus doxycycline. Treatment for gonococcal urethritis with negative *Chlamydia* is ceftriaxone alone. Patients with no gonorrhea who have *Chlamydia* are treated with azithromycin or doxycyline monotherapy.

Pharmacology Infectious Diseases Urethritis

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A 10-year-old boy is brought to the emergency department due to respiratory distress. Over the past 6 hours, rapid, noisy breathing has progressively developed. Temperature is 40.1 C (104.2 F), blood pressure is 105/75 mm Hg, pulse is 120/min, and respirations are 32/min. Examination shows inspiratory stridor and supraclavicular retractions. Lateral neck x-ray is shown in the exhibit. The patient is admitted to the hospital, and blood cultures are obtained. If blood cultures are positive, which of the following would most likely be seen on Gram stain?

A. Gram-negative cocci in pairs
B. Gram-negative coccobacilli
C. Gram-negative rods in chains
D. Gram-positive cocci in chains
E. Gram-positive cocci in clusters

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A 10-year-old boy is brought to the emergency department due to respiratory distress. Over the past 6 hours, rapid, noisy breathing has progressively developed. Temperature is 40.1 C (104.2 F), blood pressure is 105/75 mm Hg, pulse is 120/min, and respirations are 32/min. Examination shows inspiratory stridor and supraclavicular retractions. Lateral neck x-ray is shown in the exhibit. The patient is admitted to the hospital, and blood cultures are obtained. If blood cultures are positive, which of the following would most likely be seen on Gram stain?

A. ~~Gram-negative cocci in pairs~~ (2%)
B. Gram-negative coccobacilli (79%)
C. Gram-negative rods in chains (7%)
D. Gram-positive cocci in chains (6%)
E. Gram-positive cocci in clusters (3%)

Correct

79%
Answered correctly

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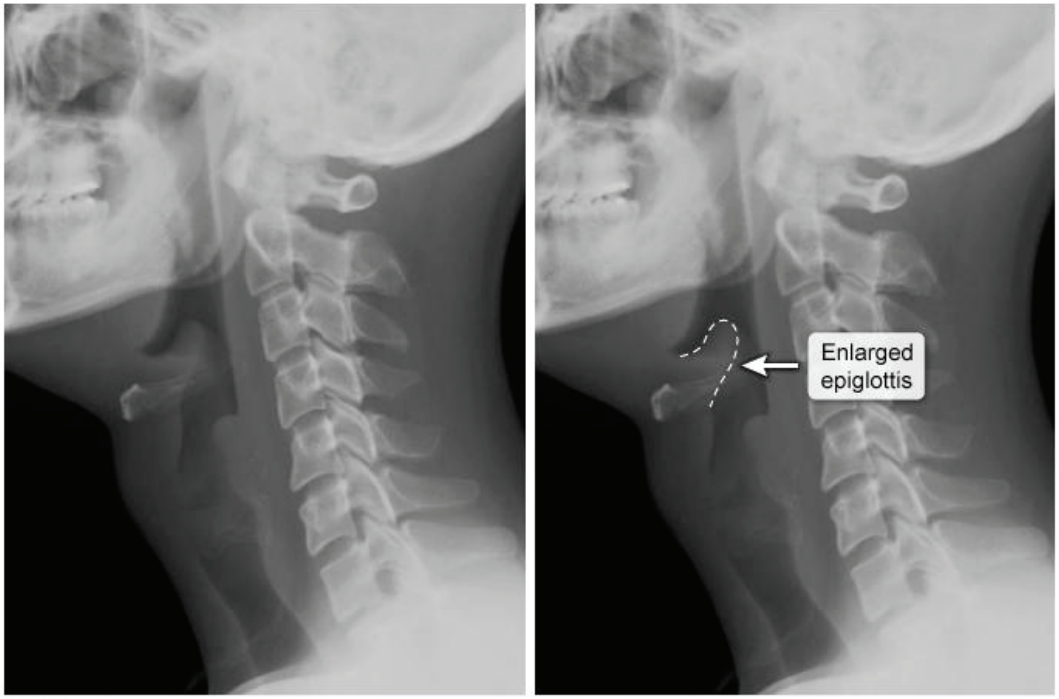
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Epiglottitis



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This child has high fever and **rapidly progressive respiratory distress** (eg, retractions, stridor) with a **swollen epiglottis** ("thumbprint sign") on lateral neck x-ray. These findings are consistent with **epiglottitis**, an uncommon but potentially fatal infection of the upper airway. Progressive epiglottic inflammation can also cause dysphagia and drooling with pooled oral secretions, and the potential for acute airway obstruction makes rapid diagnosis critical.

Epiglottitis once occurred mainly in young children (age ~3) due to high rates of infection with ***Haemophilus influenzae* type b (Hib)**. With widespread vaccination against Hib, rates of epiglottitis dramatically declined; now, adults and school-aged children are more commonly affected. *H influenzae* remains the most common pathogen, including Hib (due to waning immunity) and **nontypeable strains** for which there are no vaccines. Hib epiglottitis is often associated with concomitant **bacteremia**, and Gram stain would show gram-negative coccobacilli consistent with *H influenzae*.

(Choices A and C) Gram-negative cocci (eg, *Moraxella* in pairs) and rods (eg, *Klebsiella* in pairs or short chains) are rare causes of epiglottitis. In addition, associated bacteremia is far more likely when Hib is the causative pathogen due to its highly virulent capsule.

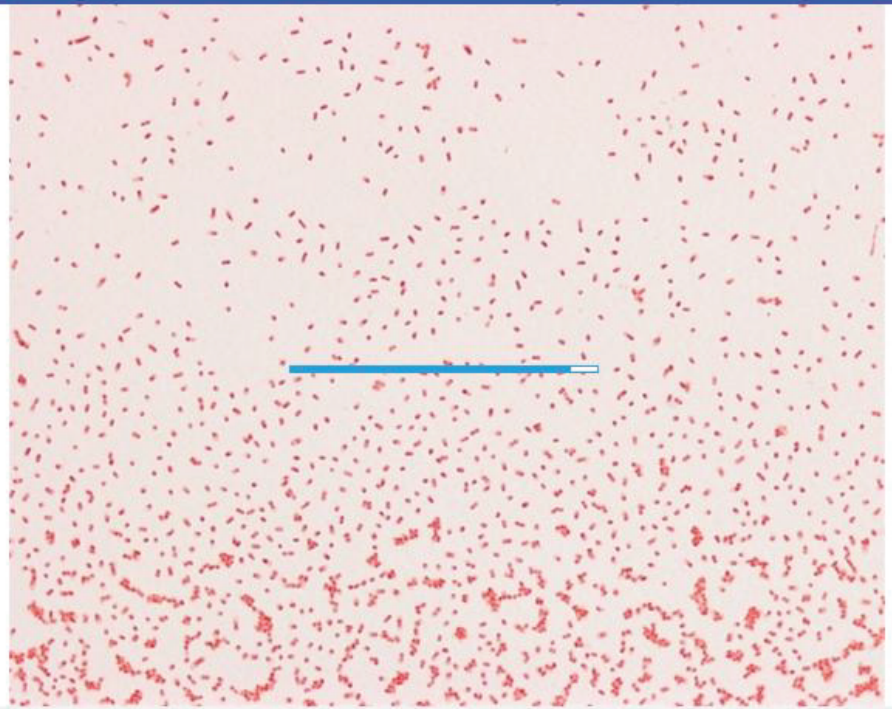
(Choices D and E) Gram-positive organisms (eg, *Streptococcus pneumoniae* in chains, *Staphylococcus aureus* in clusters) are less common causes of epiglottitis. Although the number of epiglottitis cases

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chains) are rare causes of epiglottitis. In addition, associated bacteremia is far more likely when Hib is the causative pathogen due to its highly virulent capsule.

(Choices D and E) Gram-positive organisms (eg, *Streptococcus pneumoniae* in chains, *Staphylococcus aureus* in clusters) are less common causes of epiglottitis. Although the number of epiglottitis cases caused by these organisms (particularly *S pneumoniae*) has increased since widespread vaccination against Hib, the combined strains of *H influenzae* still occur more frequently than any other organism.

Educational objective:

Epiglottitis causes rapidly progressive respiratory distress and a swollen epiglottis ("thumbprint sign") on lateral neck x-ray. The most common pathogen is *Haemophilus influenzae* (ie, type b, nontypeable strains), a gram-negative coccobacillus that often causes concomitant bacteremia.

References

- Epiglottitis.

Microbiology	Infectious Diseases	Epiglottitis
Subject	System	Topic

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www.ncbi.nlm.nih.gov/pubmed/19648510

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A scientist is conducting research to discover novel drug targets for antiretroviral agents against HIV. An HIV-positive blood sample is analyzed in the laboratory, and purified CD4 T lymphocytes are extracted. Using molecular tracing techniques, the scientist follows a viral HIV protein that is synthesized in the blood sample's T cells. The protein becomes glycosylated before being proteolytically cleaved into 2 smaller proteins in the Golgi apparatus. Which of the following best describes the function of these 2 newly formed HIV proteins?

A. Viral DNA integration into the host genome
B. Viral DNA synthesis from RNA template
C. Viral polyprotein cleavage
D. Virion attachment to the target cells
E. Virus-induced cell apoptosis

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A scientist is conducting research to discover novel drug targets for antiretroviral agents against HIV. An HIV-positive blood sample is analyzed in the laboratory, and purified CD4 T lymphocytes are extracted. Using molecular tracing techniques, the scientist follows a viral HIV protein that is synthesized in the blood sample's T cells. The protein becomes glycosylated before being proteolytically cleaved into 2 smaller proteins in the Golgi apparatus. Which of the following best describes the function of these 2 newly formed HIV proteins?

A. Viral DNA integration into the host genome (10%)
B. Viral DNA synthesis from RNA template (12%)
C. Viral polyprotein cleavage (12%)
D. Virion attachment to the target cells (61%)
E. Virus-induced cell apoptosis (3%)

Correct

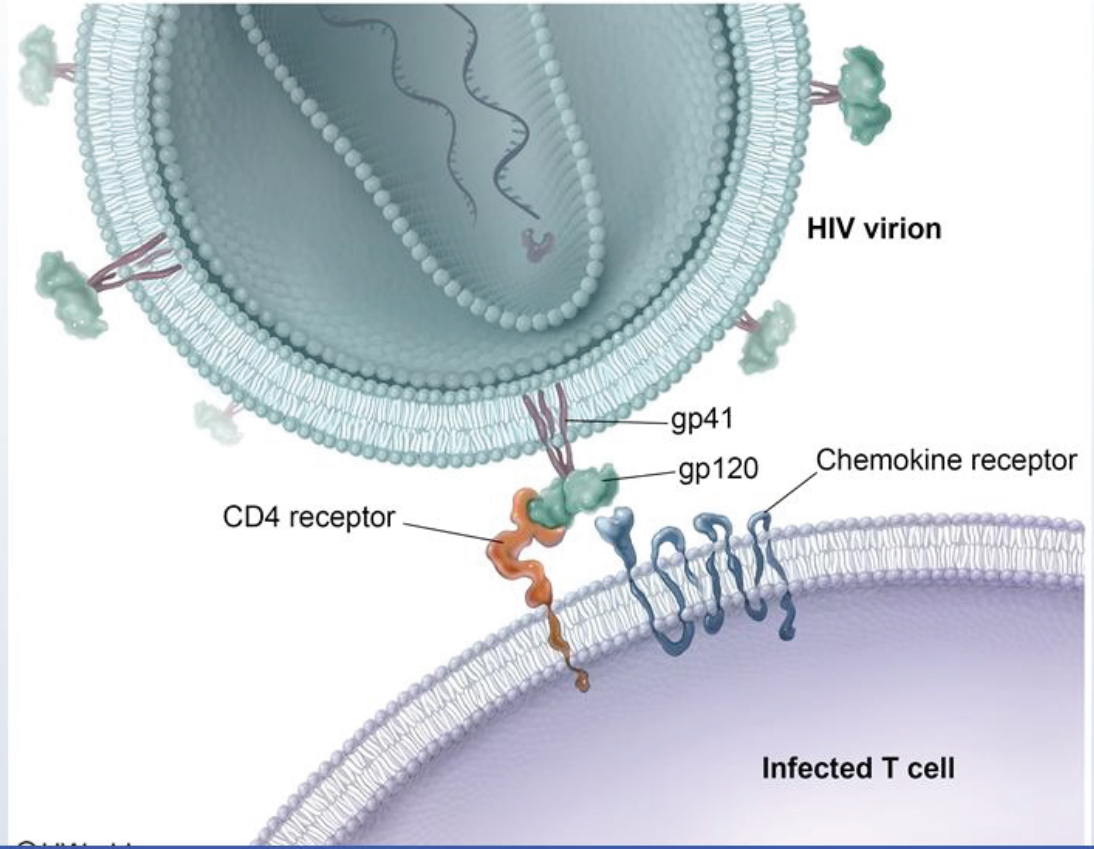
61% Answered correctly

54 secs Time Spent

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The HIV genome contains a set of structural genes (*gag*, *pol*, and *env*) that encode **polyproteins**. These polyproteins are subsequently cleaved by host or viral proteases into the individual proteins that compose the HIV virus.

The only **glycosylated** HIV polyprotein is **gp160**, the product of the *env* gene. gp160 is extensively glycosylated in the rough endoplasmic reticulum and Golgi apparatus. It is then cleaved into the envelope proteins **gp120**, which mediates viral attachment, and **gp41**, which mediates viral fusion with the host cell. Glycosylation of these proteins is crucial for:

- **Immune evasion** – Glycosylation acts as a shield for the conserved regions of these surface proteins, masking them from immune recognition.
- **Host cell binding**
- Proper protein folding

(Choices A, B, and C) The *pol* gene encodes for reverse transcriptase, integrase, and protease, three crucial HIV enzymes. Reverse transcriptase converts single-stranded viral RNA into double-stranded DNA, which is then integrated into the host genome by integrase. Protease helps cleave HIV polyproteins into individual proteins after transcription in the rough endoplasmic reticulum. These enzymes are not

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crucial HIV enzymes. Reverse transcriptase converts single-stranded viral RNA into double-stranded DNA, which is then integrated into the host genome by integrase. Protease helps cleave HIV polyproteins into individual proteins after transcription in the rough endoplasmic reticulum. These enzymes are not glycosylated.

(Choice E) Uninfected CD4 cells can undergo activation-induced apoptosis when responding to HIV peptides displayed on the surface of infected cells. CD4 cells infected with HIV are damaged primarily through direct cytopathic effects. Both mechanisms contribute to CD4 cell depletion in HIV infection.

Educational objective:

In the HIV replication cycle, polyprotein precursors are encoded by the structural genes *gag*, *pol*, and *env*. Only the *env* gene polyprotein product (gp160) is glycosylated. This polyprotein is subsequently cleaved in the Golgi apparatus to form the envelope glycoproteins gp120 and gp41.

References

- HIV-1 envelope glycoprotein biosynthesis, trafficking, and incorporation

Microbiology	Infectious Diseases	HIV
Subject	System	Topic

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A 21-year-old man is brought to the emergency department in a stuporous condition. He returned from a family visit to Mexico 2 weeks ago. One week ago, the patient began developing high-grade fever, headaches, severe myalgias, and joint pains. He had similar symptoms following a trip to Mexico 5 years ago, but at that time the symptoms did not progress and instead resolved spontaneously within a few days. Temperature is 38.3 C (101 F), blood pressure is 80/50 mm Hg, and pulse is 128/min. Examination shows a diffuse maculopapular rash, multiple purpuric lesions, and hepatomegaly. Laboratory studies show marked thrombocytopenia, leukopenia, and elevated liver aminotransferases. Which of the following is the most likely mechanism for this patient's current severe illness?

A. Antigenic drift in the virus
B. Blunted T-lymphocyte response
C. Infection with a different viral serotype
D. Larger viral inoculation dose
E. Viral superinfection

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family visit to Mexico 2 weeks ago. One week ago, the patient began developing high-grade fever, headaches, severe myalgias, and joint pains. He had similar symptoms following a trip to Mexico 5 years ago, but at that time the symptoms did not progress and instead resolved spontaneously within a few days. Temperature is 38.3 C (101 F), blood pressure is 80/50 mm Hg, and pulse is 128/min. Examination shows a diffuse maculopapular rash, multiple purpuric lesions, and hepatomegaly. Laboratory studies show marked thrombocytopenia, leukopenia, and elevated liver aminotransferases. Which of the following is the most likely mechanism for this patient's current severe illness?

A. Antigenic drift in the virus (14%)
B. Blunted T-lymphocyte response (10%)
C. Infection with a different viral serotype (45%)
D. Larger viral inoculation dose (4%)
E. Viral superinfection (25%)

Correct
45%
01 min, 36 secs
11/27/2020

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Clinical features of dengue fever	
Classic dengue fever	• Flulike febrile illness with marked myalgias & joint pains ("break-bone fever") • Retro-orbital pain • Rash ("white islands in sea of red")
Dengue hemorrhagic fever	• Increased vascular permeability • Thrombocytopenia (<100,000/mm^3) • Spontaneous bleeding → shock • Positive tourniquet test (petechiae after sphygmomanometer cuff inflation for 5 minutes)
Management	• Supportive care

This patient's presentation after recent travel to an endemic area suggests **dengue hemorrhagic fever (DHF)**. Dengue viruses are transmitted by the *Aedes* mosquito and are single-stranded RNA viruses (genus *Flavivirus*) with 4 different serotypes (DENV1-4). Primary (first) infection can be asymptomatic or cause a self-limited disease in most adults. Symptomatic disease can cause high-grade fever, headache,

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(DHF). Dengue viruses are transmitted by the *Aedes* mosquito and are single-stranded RNA viruses (genus *Flavivirus*) with 4 different serotypes (DENV1-4). Primary (first) infection can be asymptomatic or cause a self-limited disease in most adults. Symptomatic disease can cause high-grade fever, headache, retro-orbital pain, bleeding (eg, epistaxis, petechiae/purpura), diffuse macular rash, muscle and joint pain ("break-bone fever"), leukopenia, thrombocytopenia, and elevated liver enzymes.

Primary infection leads to lifelong immunity against the same serotype, but individuals can be infected with a different serotype. **Secondary** infection with a **different** viral **serotype** can cause a **more severe** illness, possibly due to antibody-dependent enhancement of infection, enhanced immune complex formation, and/or accelerated (not blunted) T-lymphocyte responses **(Choice B)**. DHF, which can be a serious manifestation of secondary infection, is due to increased capillary permeability and can be manifested by marked thrombocytopenia, prolonged fever, respiratory/circulatory failure, and shock. Patients also develop more significant hemorrhagic tendencies (eg, petechiae with tourniquet application) and spontaneous bleeding.

(Choice A) Antigenic drift refers to minor changes in viral structure that can increase the infectivity rate and lead to localized outbreaks. Antigenic drift is common annually with the influenza virus but is not typically associated with the dengue virus.

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and lead to localized outbreaks. Antigenic drift is common annually with the influenza virus but is not typically associated with the dengue virus.

(Choice D) The severity of secondary infection with dengue is usually independent of the dose of viral inoculation.

(Choice E) Viral superinfection can occur with hepatitis viruses such as hepatitis D, which usually co-infects with hepatitis B. However, secondary infection with dengue is due to a different viral serotype rather than superinfection.

Educational objective:

Dengue viruses are single-stranded RNA viruses with 4 different serotypes. Primary (first) infection can be asymptomatic or cause a self-limited disease in most adults. Secondary infection is due to infection with a different viral serotype and usually causes more severe illness.

References

- The pathology of dengue hemorrhagic fever.

Microbiology	Infectious Diseases	Dengue fever
Subject	System	Topic

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A 35-year-old woman comes to the emergency department due to an itchy rash that appeared earlier this morning. She recently returned from a family vacation at a resort in Cancun. Two days ago, the patient's husband developed similar symptoms. The patient has no significant past medical history and takes no medications. She has no known allergies. Her temperature is 37.6 C (99.7 F). On examination, there is a diffuse, pruritic, papulopustular rash that is most noticeable on the trunk and extremities. Microbiologic analysis of a pustular fluid sample demonstrates oxidase-positive gram-negative rods that produce pigment on culture medium. Which of the following is the most likely source of this patient's infection?

- A. Food
- B. Human contact
- C. Insects
- D. Pets
- E. Pool water
- F. Soil

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morning. She recently returned from a family vacation at a resort in Cancun. Two days ago, the patient's husband developed similar symptoms. The patient has no significant past medical history and takes no medications. She has no known allergies. Her temperature is 37.6 C (99.7 F). On examination, there is a diffuse, pruritic, papulopustular rash that is most noticeable on the trunk and extremities. Microbiologic analysis of a pustular fluid sample demonstrates oxidase-positive gram-negative rods that produce pigment on culture medium. Which of the following is the most likely source of this patient's infection?

A. Food (6%)
B. Human contact (5%)
C. Insects (5%)
D. Pets (1%)
E. Pool water (77%)
F. Soil (3%)

Correct

77%

01 min, 02 secs

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The clinical syndrome described is consistent with "**hot tub folliculitis**," a superficial pseudomonal infection of the hair follicle. This condition, characterized by a pruritic, papulopustular rash, is most commonly seen with outbreaks from public or hotel swimming pools or hot tubs where the chemicals in the **pool water** have not been maintained at appropriate concentrations, thereby allowing ***Pseudomonas aeruginosa*** proliferation.

P aeruginosa is ubiquitous in nature. Many *P aeruginosa* infections often begin with exposure to a **water** source or creation of a moist environment (ie, swimmer's ear, hot tub folliculitis, burn wound). *P aeruginosa* is a motile **gram-negative rod** that is **oxidase**-positive, produces green pigment (**pyocyanin**, pyoverdin) during culture, and is nearly always implicated in "hot tub folliculitis."

(Choices A, B, and C) Scabies can be transmitted by human contact but is due to a mite. *P aeruginosa* is not transmitted by food or insects.

(Choice D) Cat scratch disease is due to the oxidase-negative gram-negative *Bartonella henselae* and can present as vesicular, erythematous, or papular lesions localized to the site of primary inoculation.

(Choice F) Although *P aeruginosa* grows in soil, the most likely source of this patient's infection is exposure to water.

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(Choice D) Cat scratch disease is due to the oxidase-negative gram-negative *Bartonella henselae* and can present as vesicular, erythematous, or papular lesions localized to the site of primary inoculation.

(Choice F) Although *P aeruginosa* grows in soil, the most likely source of this patient's infection is exposure to water.

Educational objective:
"Hot tub folliculitis" is a superficial and self-limited *Pseudomonas aeruginosa* infection of the hair follicles that tends to occur in minor outbreaks following exposure to a pool or spa in which the chemicals have not been maintained at appropriate concentrations. *Pseudomonas* are gram-negative, oxidase-positive, nonlactose-fermenting, motile rods that produce green pigment.

Microbiology	Infectious Diseases	Skin and soft tissue infections
Subject	System	Topic

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A 24-year-old woman comes to the emergency department due to fevers and chills over the last 24 hours. Three weeks ago, she underwent a partial bowel resection for Crohn disease without complications. Since the surgery, the patient has had difficulty eating and has a peripherally inserted central venous catheter in place through which she is receiving parenteral nutrition. Her temperature is 38.2 C (101 F), blood pressure is 100/60 mm Hg, and pulse is 114/min. The surgical wound healed well, and her abdomen is soft and nontender. The catheter site on the left arm is mildly tender but shows no erythema. Chest x-ray reveals a properly positioned central venous line and is otherwise unremarkable. Admission blood cultures subsequently return positive for yeast. Which of the following is characteristic of the most likely organism causing this bloodstream infection?

A. Broad-based budding morphology
B. Dimorphic fungi endemic to southwestern United States
C. Positive India ink stain
D. Pseudohyphae with blastoconidia
E. Right-angle branching hyphae

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the surgery, the patient has had difficulty eating and has a peripherally inserted central venous catheter in place through which she is receiving parenteral nutrition. Her temperature is 38.2 C (101 F), blood pressure is 100/60 mm Hg, and pulse is 114/min. The surgical wound healed well, and her abdomen is soft and nontender. The catheter site on the left arm is mildly tender but shows no erythema. Chest x-ray reveals a properly positioned central venous line and is otherwise unremarkable. Admission blood cultures subsequently return positive for yeast. Which of the following is characteristic of the most likely organism causing this bloodstream infection?

A. Broad-based budding morphology (13%)

B. Dimorphic fungi endemic to southwestern United States (4%)

C. Positive India ink stain (9%)

D. Pseudohyphae with blastoconidia (58%)

E. Right-angle branching hyphae (13%)

Correct

58%

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Characteristics of pathogenic yeasts		
Organism	**Morphology**	**Clinical syndromes**
Candida	Pseudohyphae with blastoconidia	Mucocutaneous or invasive infections (eg, candidemia due to vascular catheter)
Blastomyces	Yeast with broad-based budding	Inhaled → skin & bone
Coccidioides	Spherules with endospores	Transient pulmonary syndrome → meninges & bone
Cryptococcus	Encapsulated yeast	Meningitis in immunocompromised (eg, advanced AIDS)
Histoplasma	Small, oval yeast within macrophages	Mostly subclinical but can cause community-acquired pneumonia → dissemination

This patient who has a central venous catheter and is receiving parenteral nutrition has sepsis (fever, tachycardia) with blood cultures growing yeast. Patients receiving **parenteral nutrition** (through a central venous **catheter**) are at high risk for **candidemia** (*Candida* in the bloodstream). *Candida* can colonize the

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This patient who has a central venous catheter and is receiving parenteral nutrition has sepsis (fever, tachycardia) with blood cultures growing yeast. Patients receiving **parenteral nutrition** (through a central venous **catheter**) are at high risk for **candidemia** (*Candida* in the bloodstream). *Candida* can colonize the catheter, and the lipid emulsion in the parenteral nutrition solution is thought to promote the growth of some *Candida* species. The morphology of *Candida* includes branching pseudohyphae with blastoconidia. Most species are susceptible to echinocandins, and *C albicans* is nearly always susceptible to fluconazole.

(Choice A) Broad-based budding is characteristic of ***B**lastomyces*. This organism can cause pulmonary infection and occasional dissemination, but bloodstream infection in the setting of a vascular catheter is unlikely.

(Choice B) *Coccidioides* is a dimorphic fungi endemic to the southwestern United States. This organism is inhaled and can cause pulmonary infection with occasional dissemination, particularly among immunocompromised patients.

(Choice C) *Cryptococcus* is a yeast with a thick capsule that does not absorb India ink, resulting in a clear halo that can aid in the diagnosis of cryptococcal infection. The most common cryptococcal infection is meningitis, particularly among immunocompromised patients. Fungemia in the setting of a vascular catheter is uncommon.

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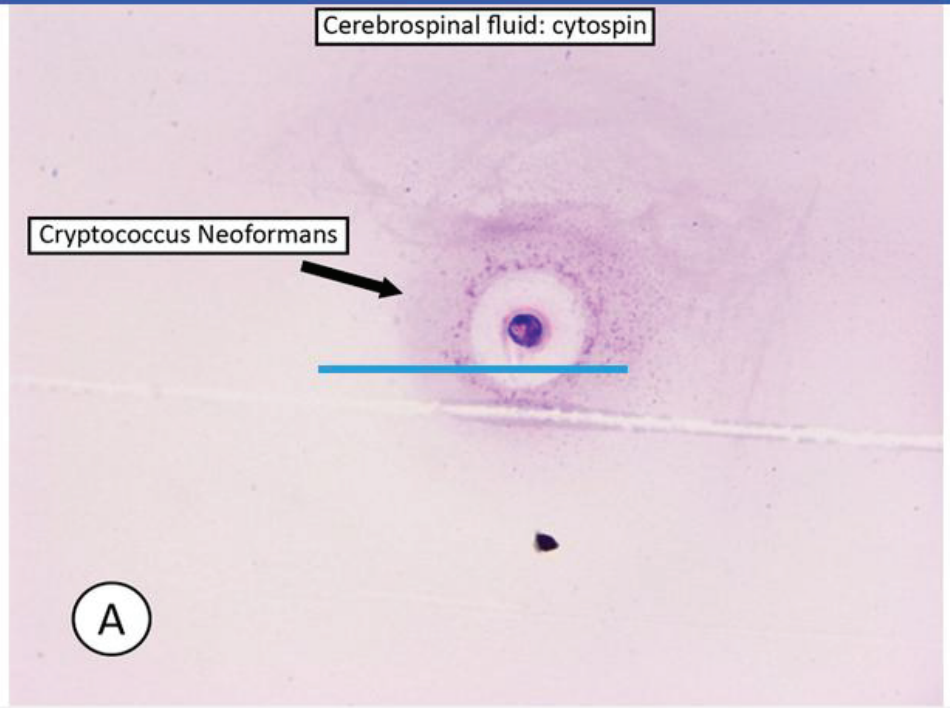


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halo that can aid in the diagnosis of cryptococcal infection. The most common cryptococcal infection is meningitis, particularly among immunocompromised patients. Fungemia in the setting of a vascular catheter is uncommon.

(Choice E) Right-angle branching hyphae are characteristic of mucormycosis, a mold infection primarily due to *Mucorales* or *Rhizopus* species. These infections can cause invasive disease in immunocompromised patients, including angioinvasive infections, but the organisms do not grow in blood cultures and are not associated with intravascular catheters.

Educational objective:

The presence of a central vascular catheter and receipt of parenteral nutrition are risk factors for candidemia. *Candida* display a morphology of branching pseudohyphae with blastoconidia.

References

- British Society for Medical Mycology best practice recommendations for the diagnosis of serious fungal diseases.
- Epidemiology of invasive mycoses in North America.

Microbiology	Infectious Diseases	Catheter related bloodstream infection
Subject	System	Topic

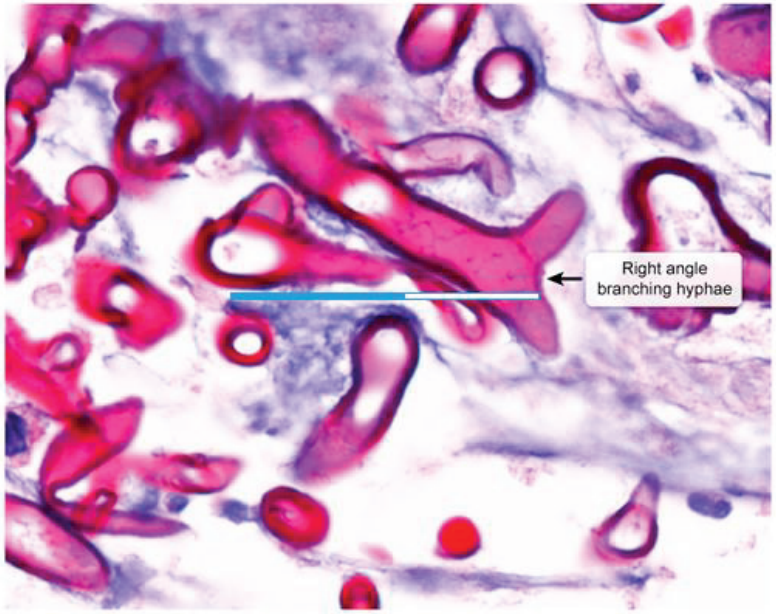
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halo that can aid in the diagnosis of cryptococcal infection. The most common cryptococcal infection is

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Invasive fungal sinusitis due to mucormycosis (zygomycosis)



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Subject | System | Topic

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A 10-month-old boy is brought to the emergency department due to 2 days of fever, irritability, and vomiting. The patient has had no prior significant medical conditions and has received all recommended vaccinations, including protein-conjugated, 13-valent pneumococcal capsular polysaccharide vaccines (PCV13) at ages 2, 4, and 6 months. On physical examination, the patient is febrile and lethargic, with a bulging anterior fontanelle. Lumbar puncture yields turbid fluid with an abundance of neutrophils. Gram stain of cerebrospinal fluid reveals lancet-shaped, gram-positive diplococci. Which of the following best explains this patient's current condition?

A. Antigenic variation of bacterial cell wall
B. Infection from capsule-lacking bacteria
C. Infection from nonvaccine serotype
D. Primary T-cell immunodeficiency
E. T-cell–independent vaccine response

Submit

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A 10-month-old boy is brought to the emergency department due to 2 days of fever, irritability, and vomiting. The patient has had no prior significant medical conditions and has received all recommended vaccinations, including protein-conjugated, 13-valent pneumococcal capsular polysaccharide vaccines (PCV13) at ages 2, 4, and 6 months. On physical examination, the patient is febrile and lethargic, with a bulging anterior fontanelle. Lumbar puncture yields turbid fluid with an abundance of neutrophils. Gram stain of cerebrospinal fluid reveals lancet-shaped, gram-positive diplococci. Which of the following best explains this patient's current condition?

A. Antigenic variation of bacterial cell wall (10%)
B. Infection from capsule-lacking bacteria (7%)
C. Infection from nonvaccine serotype (56%)
D. Primary T-cell immunodeficiency (16%)
E. T-cell–independent vaccine response (8%)

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Streptococcus pneumoniae, a gram-positive lancet-shaped diplococcus, causes life-threatening invasive infections such as pneumonia and **meningitis** (eg, fever, vomiting, bulging fontanelle). Its major virulence factor is a **polysaccharide capsule** that protects the bacterium from phagocytosis and opsonization. Antigenic variation in the polysaccharide capsule differentiates >93 *S pneumoniae* serotypes. Immunity against one provides little or no protection against others. Therefore, infection with a new serotype typically leads to weeks/months of nasopharyngeal colonization and increased risk of invasive infection.

Vaccination against the most common and virulent *S pneumoniae* serotypes is recommended for children and high-risk adults to reduce colonization and invasive disease. In children, a 13-valent pneumococcal capsular **polysaccharide-conjugate vaccines** (PCV13) is typically administered; this vaccine contains polysaccharides from 13 serotypes conjugated to an **immunogenic carrier protein** (nontoxic recombinant diphtheria toxin) to improve immunogenicity.

Although vaccination creates protective antibodies against included polysaccharide antigens, it provides little or no protection against strains not in the vaccine; therefore, invasive disease with a **nonvaccinated serotype** can still occur.

(Choice A) Antigenic variation in the bacterial cell wall can lead to short-lived immunity against certain

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serotype can still occur.

(Choice A) Antigenic variation in the bacterial cell wall can lead to short-lived immunity against certain bacteria (eg, *Neisseria gonorrhoeae*). In contrast, *S pneumoniae* antigenic variation occurs primarily on the polysaccharide capsule, not the cell wall.

(Choice B) Some *S pneumoniae* strains have no polysaccharide capsule; these strains are minimally virulent and rarely cause invasive disease.

(Choice D) T-cell immunodeficiency would likely increase the risk for poor response to vaccinations. However, primary T-cell immunodeficiency is quite rare and typically presents with recurrent upper respiratory infections. This patient is far more likely to be infected with a strain not in the vaccine.

(Choice E) The 23-valent pneumococcal polysaccharide vaccine (PPSV23) contains capsular polysaccharide antigens with no protein conjugate; therefore, it elicits a T-cell–independent response and is not immunogenic enough to be used in individuals age <2. PPSV23 is reserved primarily for high-risk adults.

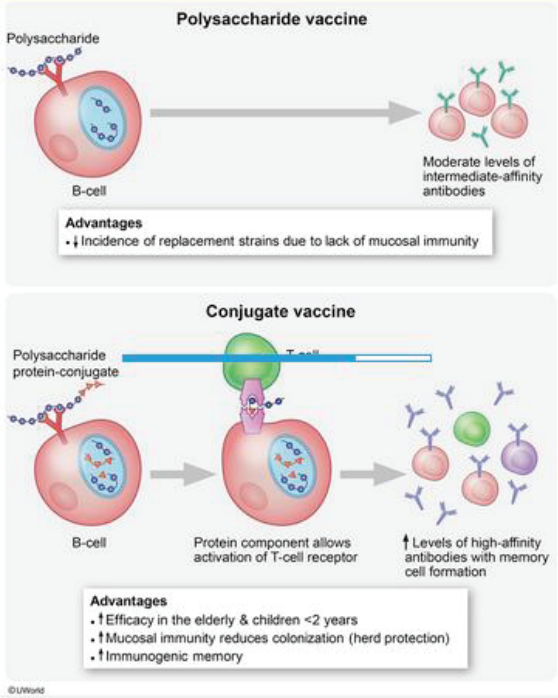
Educational objective:

Streptococcus pneumoniae is virulent primarily due to a polysaccharide capsule. A conjugant vaccine provides long-lasting immunity against serotypes in the vaccine but provides no significant immunity

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virulent and rarely cause invasive disease.

(Choice D) T-cell immunodeficiency would likely increase the risk for poor response to vaccinations. However, primary T-cell immunodeficiency is quite rare and typically presents with recurrent upper respiratory infections. This patient is far more likely to be infected with a strain not in the vaccine.

(Choice E) The 23-valent pneumococcal polysaccharide vaccine (PPSV23) contains capsular polysaccharide antigens with no protein conjugate; therefore, it elicits a T-cell–independent response and is not immunogenic enough to be used in individuals age <2. PPSV23 is reserved primarily for high-risk adults.

Educational objective:

Streptococcus pneumoniae is virulent primarily due to a polysaccharide capsule. A conjugant vaccine provides long-lasting immunity against serotypes in the vaccine but provides no significant immunity against nonvaccinated serotypes. Therefore, infection can still occur due to serotypes not covered by the vaccine.

Microbiology	Infectious Diseases	Streptococcus pneumoniae
Subject	System	Topic

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A 67-year-old man comes to the emergency department with low-grade fevers and fatigue. He has no history of heart disease. His temperature is 38.4 C (101.1 F), blood pressure is 117/76 mm Hg, pulse is 82/min, and respirations are 14/min. On examination, there is a diastolic murmur at the left sternal border. He has nontender erythematous macules on his hands and feet. Blood cultures show gram-positive cocci that are catalase-negative and able to grow in hypertonic (6.5%) saline and bile. This patient's medical history is most likely to include which of the following procedures within the past month?

A. Cystoscopy
B. Dental extraction
C. Nasal polypectomy
D. Sinus drainage
E. Skin biopsy

Submit

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A 67-year-old man comes to the emergency department with low-grade fevers and fatigue. He has no history of heart disease. His temperature is 38.4 C (101.1 F), blood pressure is 117/76 mm Hg, pulse is 82/min, and respirations are 14/min. On examination, there is a diastolic murmur at the left sternal border. He has nontender erythematous macules on his hands and feet. Blood cultures show gram-positive cocci that are catalase-negative and able to grow in hypertonic (6.5%) saline and bile. This patient's medical history is most likely to include which of the following procedures within the past month?

- A. Cystoscopy (39%)
- B. ~~Dental extraction~~ (52%)
- C. ~~Nasal polypectomy~~ (2%)
- D. ~~Sinus drainage~~ (2%)
- E. ~~Skin biopsy~~ (2%)

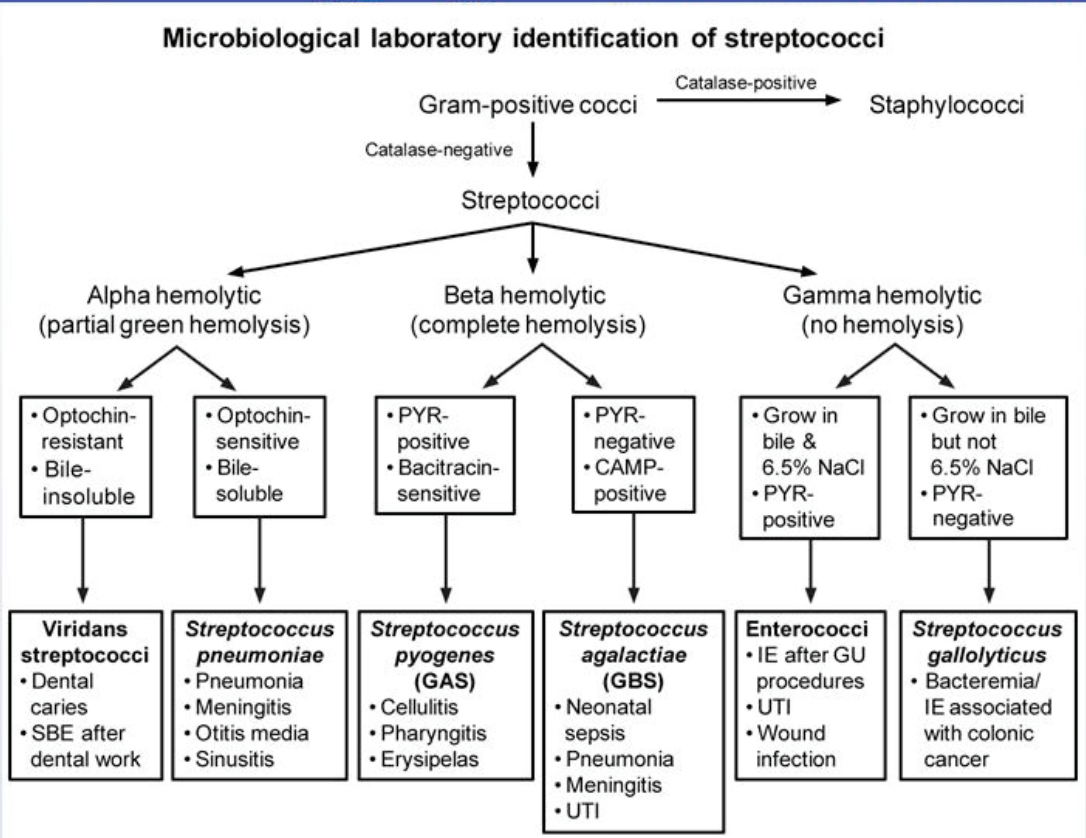
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39% Answered correctly

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A number of species were formally reclassified from the genus *Streptococcus* to the genus *Enterococcus*, but enterococci are included here under streptococci for simplicity.

CAMP = Christie, Atkins, and Munch-Petersen test; **GAS** = group A streptococci; **GBS** = group B streptococci; **GU** = genitourinary; **IE** = infective endocarditis; **NaCl** = sodium chloride; **PYR** = pyrrolidonyl arylamidase; **SBE** = subacute bacterial endocarditis; **UTI** = urinary tract infection.

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Enterococcal endocarditis (representing up to 30% of nosocomial endocarditis cases) usually occurs in elderly men who have recently undergone manipulation of areas colonized by this organism. The genitourinary tract (eg, cystoscopy) is the most common portal of entry; gastrointestinal (eg, colonoscopy) or obstetric procedures are also risk factors. Enterococci can also cause urinary tract infections (most common), intraabdominal and pelvic infections, and wound infections. Enterococci are typically gamma-hemolytic (no hemolysis on agar), **catalase-negative**, pyrrolidonyl arylamidase-positive, Lancefield Group D **gram-positive cocci** that can grow in **hypertonic (6.5%) saline and bile**. The most common species of enterococci (formerly classified under the genus *Streptococcus*) are *Enterococcus faecalis* (80%-90%) and *Enterococcus faecium* (10%-15%).

Enterococci are resistant to many antibiotics and can be very difficult to treat. A cell wall-active agent (such as ampicillin) is often combined with an aminoglycoside for synergistic effect, but increasingly bacteria resistant to both aminoglycosides and β-lactams (including penicillinase-resistant types) are emerging. Strains with vancomycin or linezolid resistance have also appeared

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Strains with vancomycin or linezolid resistance have also appeared.

(Choice B) Dental extraction is associated with endocarditis caused by viridans group streptococci (VGS). In most cases, VGS cause subacute bacterial endocarditis in already abnormal heart valves (eg, congenital valvular abnormalities, valves damaged by rheumatic fever). VGS do not grow on hypertonic saline. In addition, almost all VGS species do not grow on bile (VGS are also considered bile-insoluble as they exhibit no cell lysis in the presence of bile, in contrast to the bile-soluble *S pneumoniae*).

(Choice C) Removal of a nasal polyp can cause transient bacteremia. Organisms that colonize the nose include *Corynebacterium* species, *Haemophilus* species, staphylococci, streptococci, and *Neisseria* species. Of these, staphylococci and streptococci may cause endocarditis, but the organism described displays characteristics of *Enterococcus*.

(Choice D) Sinus infections are usually caused by *S pneumoniae, Haemophilus influenzae*, or *Moraxella catarrhalis*. *S pneumoniae* would be a very rare cause of endocarditis and is usually identified by being bile-soluble and optochin-sensitive.

(Choice E) Skin biopsy is a benign procedure that would be unlikely to cause endocarditis. Skin is colonized with many bacteria, including *Staphylococcus* and *Streptococcus* species, *Corynebacterium* species, and *Bacillus* species.

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(Choice D) Sinus infections are usually caused by *S pneumoniae, Haemophilus influenzae*, or *Moraxella catarrhalis*. *S pneumoniae* would be a very rare cause of endocarditis and is usually identified by being bile-soluble and optochin-sensitive.

(Choice E) Skin biopsy is a benign procedure that would be unlikely to cause endocarditis. Skin is colonized with many bacteria, including *Staphylococcus* and *Streptococcus* species, *Corynebacterium* species, and *Bacillus* species.

Educational objective:

Enterococcus is a component of the normal colonic and urogenital flora and is capable of growing in hypertonic saline and bile. It is gamma-hemolytic, catalase-negative, and pyrrolidonyl arylamidase-positive. Genitourinary instrumentation or catheterization has been associated with enterococcal endocarditis.

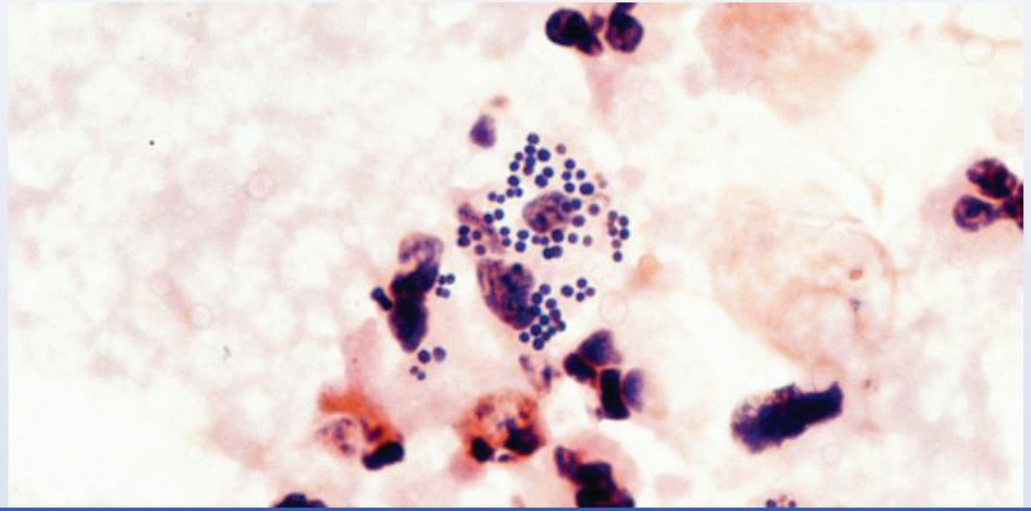
References

- Enterococcal endocarditis on native and prosthetic valves: A review of clinical and prognostic factors

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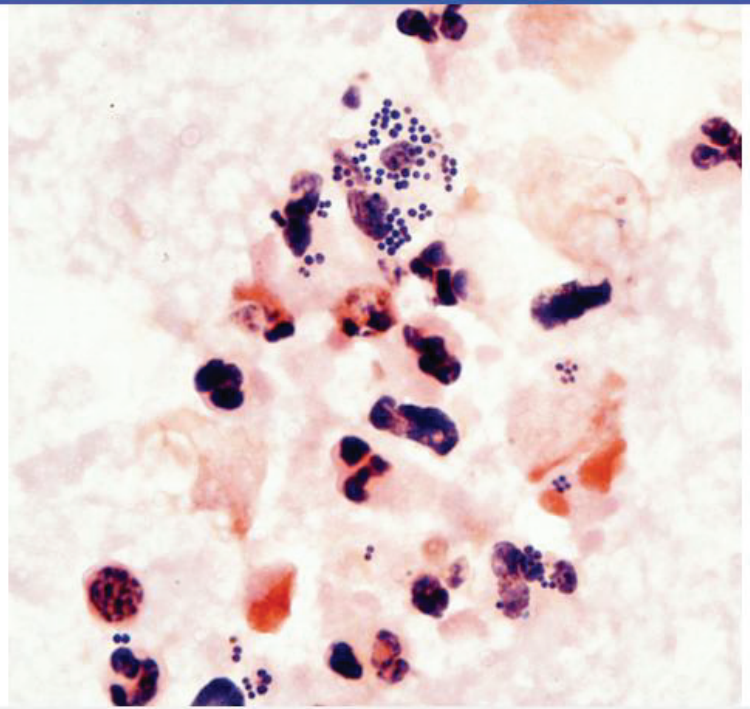
A 22-year-old man comes to the office due to a painful lesion on his upper back. The patient developed a small tender papule a few days ago that progressively enlarged and became red and painful. He has had 3 similar lesions on his upper back over the past 6 months, which were treated with incision and drainage and antibiotics. The patient has no other medical issues and takes no medications. He does not use tobacco, alcohol, or illicit drugs. On physical examination, there is a 3-cm tender pustule with surrounding erythema on his right upper back. Gram staining of purulent drainage from the lesion is shown below.



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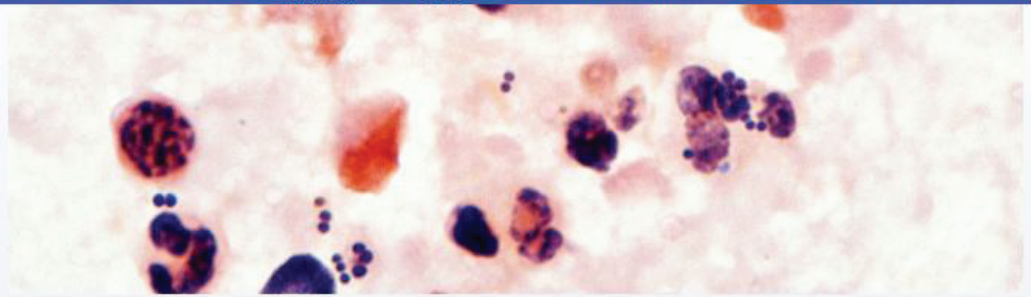
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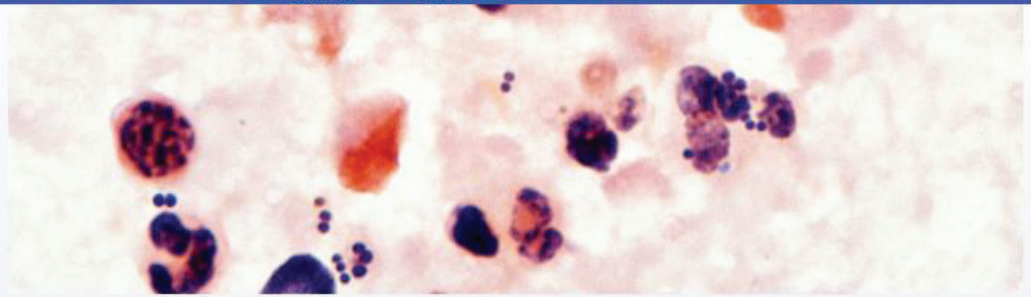


Which of the following most likely predisposed this patient to recurrent infections?

- A. Colonization in anterior nares
- B. Dormant infection in granulomas
- C. Formation of elementary bodies
- D. Harborage in epidermal burrows
- E. Spores from contaminated surfaces

Submit

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Which of the following most likely predisposed this patient to recurrent infections?

- A. Colonization in anterior nares (50%)
- B. ~~Dormant infection in granulomas~~ (10%)
- C. ~~Formation of elementary bodies~~ (13%)
- D. ~~Harborage in epidermal burrows~~ (19%)
- E. ~~Spores from contaminated surfaces~~ (6%)

Correct

50%

01 min, 11 secs

03/10/2021

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Staphylococcus aureus is a gram-positive bacterium that grows in grape-like clusters. Approximately 30% of individuals in the community-setting are colonized with *S aureus*. The pathogen is transmitted by direct contact, **colonizes the anterior nares**, and spreads to the skin. Defects in the mucosal or cutaneous barrier can lead to invasion. The most common manifestation is **skin and soft-tissue abscess**; patients usually develop a localized pustule that evolves over days into a painful nodule with a necrotic, purulent center and surrounding indurated erythema. Treatment with incision/drainage and oral antibiotics is usually curative of the localized infection. However, oral antibiotics do not eliminate *S aureus* colonization of the nares and skin so **recurrent infections** are common.

Colonization with methicillin-sensitive *S aureus* (MSSA) is associated with a low risk of illness. In contrast, methicillin-resistant *S aureus* (MRSA) colonization is much more likely to cause disease due to expression of associated virulence factors (eg, leukocidin).

(Choice B) Latent *Mycobacterium tuberculosis* is characterized by the presence of organisms in walled-off granulomas. Patients with latent tuberculosis are asymptomatic and most will never have reactivation of disease. Reactivation is classically characterized by the formation of apical, cavitary lesions in the lung, weight loss, and cough.

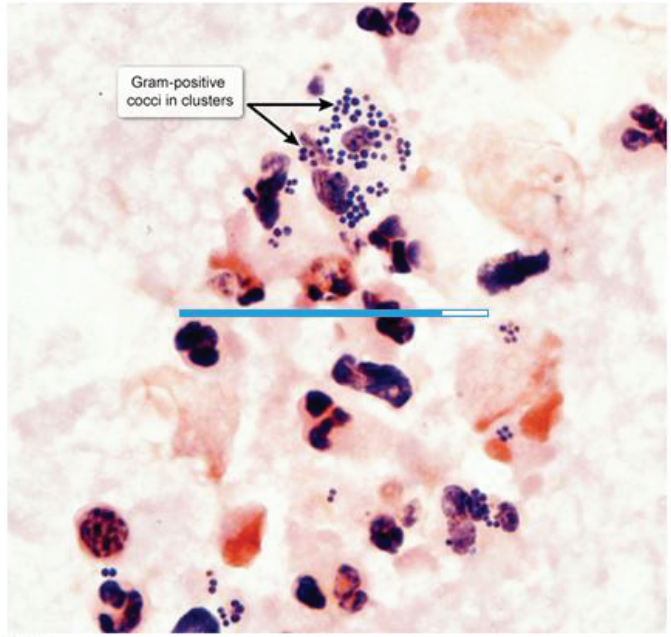
(Choice C) *Chlamydia trachomatis* is an obligate intracellular organism that invades as a small elementary

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Staphylococcus aureus



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(Choice C) *Chlamydia trachomatis* is an obligate intracellular organism that invades as a small elementary

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(Choice C) *Chlamydia trachomatis* is an obligate intracellular organism that invades as a small elementary

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(Choice C) *Chlamydia trachomatis* is an obligate intracellular organism that invades as a small elementary body and then evolves to the metabolically active reticulate body once inside host cells. Recurrent *Chlamydia* symptoms (eg, dysuria, purulent urethra discharge) in patients who have been adequately treated (eg, azithromycin) usually indicates a new infection due to continued high-risk behavior (eg, unprotected sex).

(Choice D) Scabies is a skin mite (*Sarcoptes scabiei*) that causes intensely pruritic eruptions, particularly of the finger webs, wrists, axilla, areola, and genitalia. The mite burrows into the epidermis and lays eggs. Topical treatment with permethrin is usually curative, but recurrence can occur if close contacts and environmental harbors (eg, sheets) are not adequately treated.

(Choice E) *Clostridium difficile* spores are hardy and resistant to heat and soap. Infection usually causes colitis with watery diarrhea, fever, and abdominal pain. Recurrent infection after treatment with oral antibiotics (eg, vancomycin) is common and may require a repeat pharmacologic treatment or, in some cases, fecal transplant.

Educational objective:

Staphylococcus aureus is the most common cause of skin and soft-tissue abscess (eg, furuncle). Treatment of the abscess with incision and drainage and antibiotics can eliminate the local infection but

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unprotected sex).

(Choice D) Scabies is a skin mite (*Sarcoptes scabiei*) that causes intensely pruritic eruptions, particularly of the finger webs, wrists, axilla, areola, and genitalia. The mite burrows into the epidermis and lays eggs. Topical treatment with permethrin is usually curative, but recurrence can occur if close contacts and environmental harbors (eg, sheets) are not adequately treated.

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Educational objective:
Staphylococcus aureus is the most common cause of skin and soft-tissue abscess (eg, furuncle). Treatment of the abscess with incision and drainage and antibiotics can eliminate the local infection but does not eliminate colonization of the anterior nares and skin. Therefore, recurrent infections are common.

Microbiology	Infectious Diseases	Skin and soft tissue infections
Subject	System	Topic

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A 52-year-old woman comes to the office due to worsening skin lesions on her right hand. The patient injured her hand while cleaning decaying vegetation from her rose garden 3 weeks ago. She washed the wound with soap and water and noticed a mildly itchy papule several days later. The lesion progressively enlarged, and 2 other similar papules appeared proximal to the original lesion. The patient has had no fever, chills, or severe pain. She has no previous medical conditions and takes no medications. The patient lives in the southeastern United States and has not traveled recently. Physical examination shows a 1-cm, nontender, red nodule on the dorsum of the right hand with 2 smaller papules in linear distribution proximal to it. Which of the following histopathologic findings is most likely present in this patient's skin lesions?

A. Dense inflammatory infiltrate surrounding sulfur granules
B. Granulomas with amastigote parasites inside dermal macrophages
C. Mixed granulomatous and neutrophilic inflammatory reaction
D. Perivascular lymphocytic inflammation and epidermal spongiosis
E. Prominent plasma cell infiltrates and obliterative endarteritis

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wound with soap and water and noticed a mildly itchy papule several days later. The lesion progressively enlarged, and 2 other similar papules appeared proximal to the original lesion. The patient has had no fever, chills, or severe pain. She has no previous medical conditions and takes no medications. The patient lives in the southeastern United States and has not traveled recently. Physical examination shows a 1-cm, nontender, red nodule on the dorsum of the right hand with 2 smaller papules in linear distribution proximal to it. Which of the following histopathologic findings is most likely present in this patient's skin lesions?

A. Dense inflammatory infiltrate surrounding sulfur granules (3%)

B. ~~Granulomas with amastigote parasites inside dermal macrophages~~ (4%)

C. Mixed granulomatous and neutrophilic inflammatory reaction (55%)

D. ~~Perivascular lymphocytic inflammation and epidermal spongiosis~~ (34%)

E. ~~Prominent plasma cell infiltrates and obliterative endarteritis~~ (1%)

Correct

55%

02 mins, 29 secs

03/24/2021

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Sporotrichosis is caused by ***Sporothrix schenckii***, a dimorphic fungus found in **soil** and plant matter that may be **traumatically inoculated** into the skin (eg, thorn prick) during outdoor activities (eg, **gardening**, landscaping). A mildly pruritic, erythematous, ulcerated **papule** often forms at the inoculation site (eg, hand, forearm) within weeks. As the organism spreads, **additional lesions** may develop **along the draining lymphatic chain** (ie, nodular lymphangitis).

Biopsy of the lesions reveals mixed inflammation, including **granulomas** and neutrophilic **microabscesses** in the dermis and subcutaneous tissue. Stains for fungal organisms may highlight rare, cigar-shaped yeast. The gold standard for definitive diagnosis is culture.

Sporotrichosis is typically limited to the skin and soft tissue, but disseminated infection may develop in immunocompromised individuals. **Itraconazole** is the preferred treatment for lymphocutaneous sporotrichosis.

(Choice A) Histologic features of actinomycosis include sulfur granules (aggregates of *Actinomyces* filaments) surrounded by a dense inflammatory infiltrate. Actinomycosis most commonly presents as a firm cervicofacial (eg, mandibular) mass with abscess and sinus tract formation after surgery (eg, tooth extraction) or trauma.

(Choice B) Cutaneous leishmaniasis is histologically characterized by granulomatous inflammation and

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Sporotrichosis



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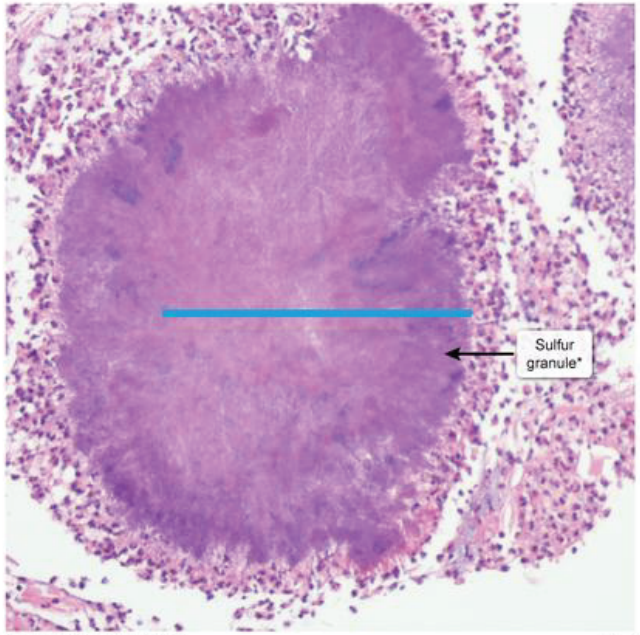
(Choice B) Cutaneous leishmaniasis is histologically characterized by granulomatous inflammation and

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Actinomycosis



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(Choice B) Cutaneous leishmaniasis is histologically characterized by granulomatous inflammation and

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(Choice B) Cutaneous leishmaniasis is histologically characterized by granulomatous inflammation and intracellular amastigote organisms within macrophages. Although it may present with ulcerated papules and nodules, cutaneous leishmaniasis is most frequently seen in the Middle East and Central and South America; this patient lives in the southeastern United States and has not traveled recently.

(Choice D) Spongiosis (ie, epidermal intercellular edema) and superficial dermal perivascular inflammation are histologic features of acute eczematous dermatitis, such as allergic contact dermatitis (eg, poison ivy). Clinical manifestations typically include erythematous, pruritic papules and vesicles, rather than nodular lesions.

(Choice E) Prominent plasma cell infiltrates and obliterative endarteritis are characteristic of syphilitic lesions. Depending on the stage of infection, cutaneous syphilitic lesions may include painless ulcers (eg, chancre), gray-white plaques (eg, condylomata lata), a maculopapular rash, and gummas.

Educational objective:
Sporotrichosis typically presents as papulonodular lesions distributed along the lymphatics and is histologically characterized by granulomatous and neutrophilic inflammation. It is caused by the dimorphic fungus *Sporothrix schenckii*, which is often inoculated into the skin during outdoor activities such as gardening.

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Cutaneous leishmaniasis



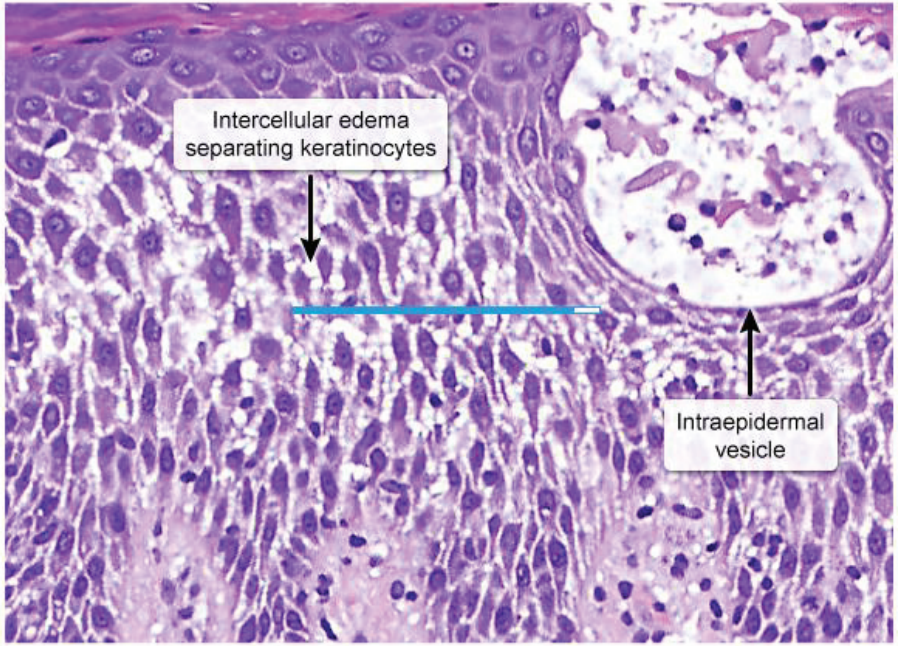
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Spongiosis



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Poison ivy



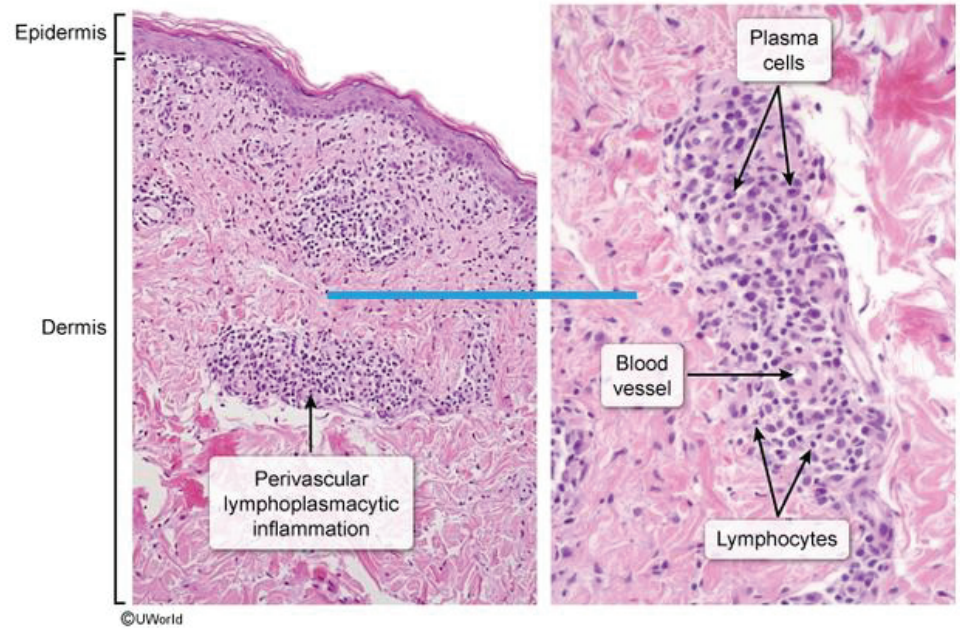
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Syphilis



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Exhibit Display

Secondary syphilis



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A 64-year-old man comes to the office due to 3 days of diarrhea. He began to have nausea, vomiting, abdominal cramps, and diarrhea 24 hours after eating chicken salad at a fast-food restaurant. The patient continues to have 4-6 episodes of diarrhea per day with no blood in the stool. His wife, who ate the same food, had a few loose stools but felt well afterward. The patient takes a tumor necrosis factor inhibitor for psoriatic arthritis and a proton pump inhibitor for gastritis. Temperature is 38 C (100.4 F), blood pressure is 120/70 mm Hg, and pulse is 88/min. Abdominal examination reveals mild diffuse tenderness to palpation and increased bowel sounds. Cultures of the stool yield gram-negative bacilli that are non-lactose fermenting and oxidase negative. Which of the following is the most likely complication associated with this patient's current infection?

A. Chronic malabsorption
B. Generalized seizure
C. Guillain-Barré syndrome
D. Hemolytic uremic syndrome
E. Long-bone osteomyelitis

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continues to have 4-6 episodes of diarrhea per day with no blood in the stool. His wife, who ate the same food, had a few loose stools but felt well afterward. The patient takes a tumor necrosis factor inhibitor for psoriatic arthritis and a proton pump inhibitor for gastritis. Temperature is 38 C (100.4 F), blood pressure is 120/70 mm Hg, and pulse is 88/min. Abdominal examination reveals mild diffuse tenderness to palpation and increased bowel sounds. Cultures of the stool yield gram-negative bacilli that are non-lactose fermenting and oxidase negative. Which of the following is the most likely complication associated with this patient's current infection?

A. Chronic malabsorption (16%)
B. Generalized seizure (4%)
C. Guillain-Barré syndrome (15%)
D. Hemolytic uremic syndrome (15%)
✓ E. Long-bone osteomyelitis (48%)

Correct
48%
01 min, 40 secs
12/11/2020

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	Nontyphoidal *Salmonella*	Typhoidal *Salmonella*
Epidemiology	• *S enterica* • **Poultry/eggs**, exotic pets • **Foodborne** (primarily) • Industrialized countries	• *S typhi*, *S paratyphi* • Humans only • Water/food contamination • **Developing countries**
Pathophysiology	Invasion of enterocytes → massive neutrophil-mediated inflammatory response in lamina propria/Peyer's patches → control of infection (usually)	Invasion of enterocytes → blunted neutrophil response due to **capsular antigen Vi** → extensive intracellular replication in macrophages → spread through lymphatics and RES
Manifestations	**Gastroenteritis** • Self-limited watery diarrhea • Rarely invasive (<5%): osteomyelitis, mycotic aneurysm, endocarditis	**Typhoid fever** • Progressive fever (pulse-temperature dissociation) • Rose spots, abdominal pain • HSM, GI bleed, perforation

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	endocarditis	HSM, GI bleed, perforation

GI = gastrointestinal; **HSM** = hepatosplenomegaly; **RES** = reticuloendothelial system.

Salmonella species are enteric gram-negative bacilli that are oxidase negative and generally non-lactose fermenting. Nontyphoidal strains such as *S enterica* are a major cause of **foodborne gastroenteritis**; there are an estimated 2-4 million cases in the United States annually. Transmission typically occurs after the consumption of contaminated **poultry products** (eg, chicken salad), including eggs. However, handling amphibians and reptiles can also lead to infection.

Ingested *Salmonella* must survive the acidic environment of the stomach prior to traveling to the small intestine to cause disease. Therefore, patients on acid suppression (eg, proton pump inhibitors) require smaller infectious doses and are generally at greater risk. In the small intestine, the organism swims through the mucus barrier, attaches to and penetrates enterocytes, and then travels within vacuoles from the apical end to the basolateral membrane and on to the lamina propria. Here, the pathogen is phagocytosed by macrophages and neutrophils and elicits a profound inflammatory response.

Manifestations may be quite mild or may feature fever, nausea, vomiting, and watery diarrhea. Most cases resolve spontaneously within 3-4 days, but a minority of individuals develop **invasive disease** with spread through the bloodstream and reticuloendothelial system. **Long-bone osteomyelitis** is a common

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complication, particularly at sites of prior bone injury/prosthesis or in those with sickle cell disease. Endocarditis, mycotic aneurysm, and visceral abscesses can also occur. The risk of invasion is greatest in patients at the extremes of age and in those with **impaired immunity** (eg, AIDS, tumor necrosis factor-alpha inhibitor).

(Choice A) Chronic malabsorption can occur with *Giardia* infection due to blunting of the small intestine villi. *Giardia* is usually acquired from contaminated water, and symptoms (watery diarrhea, foul-smelling stool, bloating, nausea) typically begin >7 days after transmission.

(Choice B) Generalized seizures are often seen in children infected with *Shigella* and are thought to be due to the systemic absorption of *Shigella* enterotoxins. *Shigella* is often transmitted in day care centers but may be passed via contaminated vegetables. Infections are typically marked by high fever, abdominal pain, and hemorrhagic colitis.

(Choice C) Guillain-Barré syndrome is most often caused by preceding *Campylobacter jejuni* infection. Although *Campylobacter* is often transmitted by poultry and can cause a clinical illness similar to *Salmonella*, the organism is oxidase positive.

(Choice D) Hemolytic uremic syndrome is characterized by the triad of acute renal insufficiency, thrombocytopenia, and microangiopathic hemolytic anemia. It is frequently linked to infections with

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(Choice C) Guillain-Barré syndrome is most often caused by preceding *Campylobacter jejuni* infection. Although *Campylobacter* is often transmitted by poultry and can cause a clinical illness similar to *Salmonella*, the organism is oxidase positive.

(Choice D) Hemolytic uremic syndrome is characterized by the triad of acute renal insufficiency, thrombocytopenia, and microangiopathic hemolytic anemia. It is frequently linked to infections with enterohemorrhagic *Escherichia coli*, a gram-negative, lactose-fermenting organism. *E coli* is typically transmitted through consumption of contaminated, undercooked ground beef and is usually associated with bloody diarrhea.

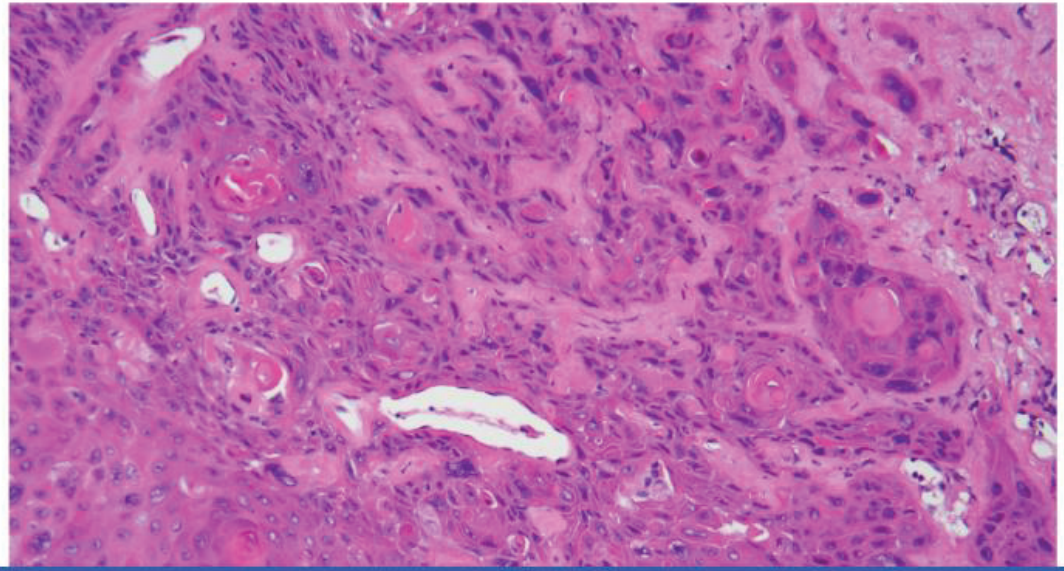
Educational objective:

Nontyphoidal *Salmonella* is a leading cause of foodborne gastroenteritis. Most cases are marked by 3-4 days of self-limited fever, nausea, vomiting, and watery diarrhea. A minority of individuals develop subsequent invasive disease with spread to the long bones (osteomyelitis), vasculature (mycotic aneurysm), or heart (endocarditis). Risk of invasion is greatest in those with sickle cell disease or impaired immunity or at the extremes of age.

Microbiology	Infectious Diseases	Acute diarrhea
Subject	System	Topic

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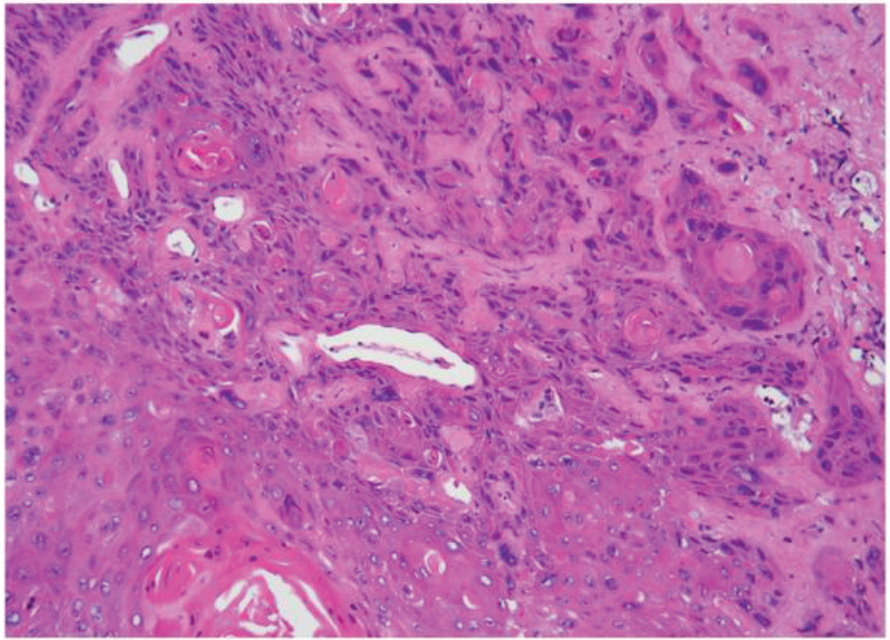
A 45-year-old man comes to the office due to a sore throat for the past 3 months. The patient also has pain with swallowing. He has never smoked, drinks alcohol occasionally, and does not use illicit drugs. On physical examination, the right tonsil is enlarged with a small area of ulceration. The rest of the physical examination is unremarkable. Biopsy of the right tonsil is shown in the image below:



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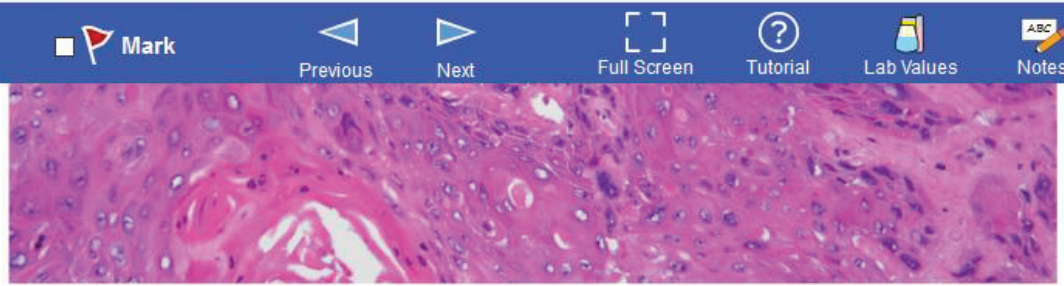
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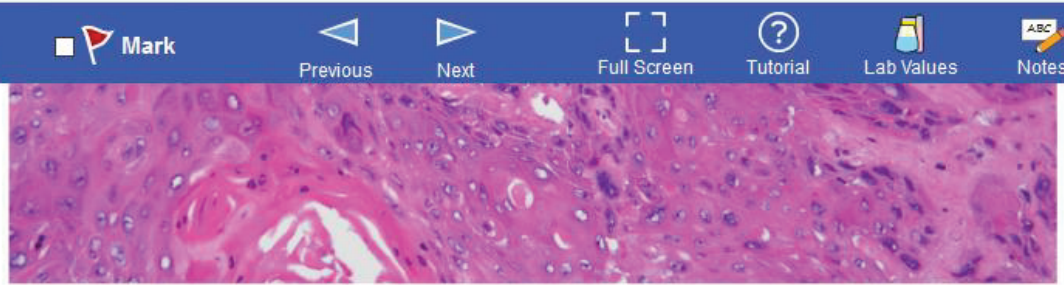
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Which of the following most likely played the most significant role in the pathogenesis of this patient's condition?

A. Coxsackievirus
B. Epstein-Barr virus
C. Herpes simplex virus
D. Human immunodeficiency virus
E. Human papilloma virus

Submit

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Which of the following most likely played the most significant role in the pathogenesis of this patient's condition?

- A. Coxsackievirus (4%)
- ✗ B. Epstein-Barr virus (35%)
- C. Herpes simplex virus (12%)
- D. Human immunodeficiency virus (5%)
- ✓ E. Human papilloma virus (41%)

Incorrect
Correct answer

41%
Answered correctly

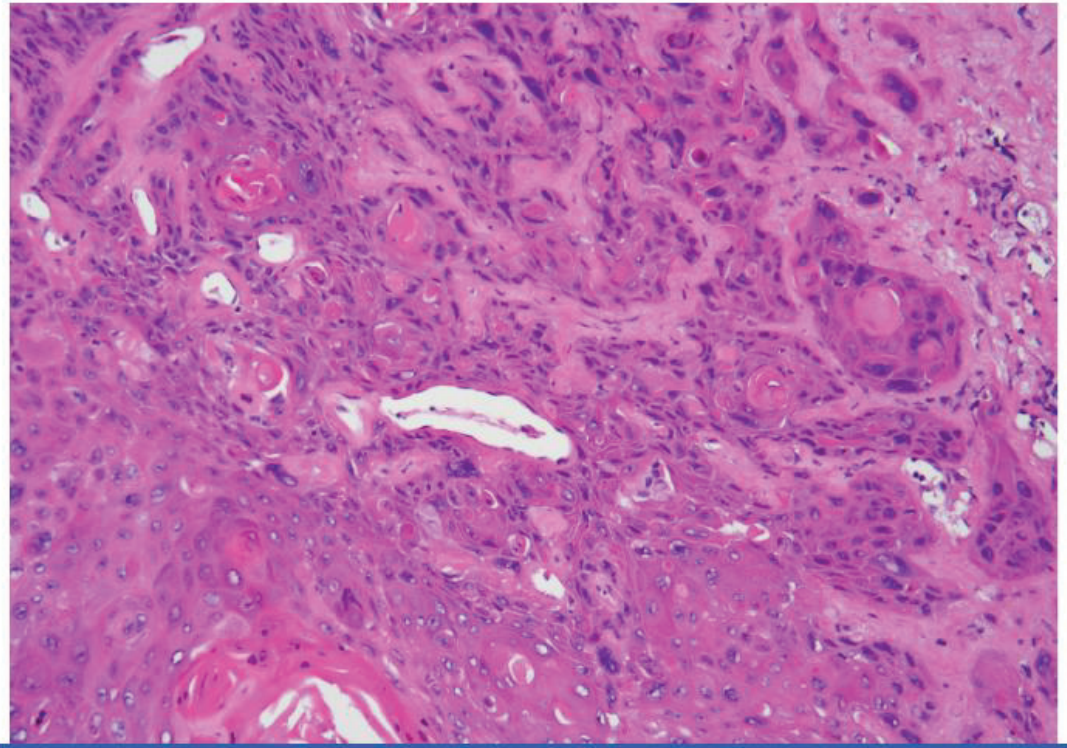
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Keratinizing squamous cell carcinoma



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Biopsy of the ulcerative tonsil lesion in this patient with persistent throat pain shows malignant cells with atypical mitotic figures and keratin pearls, findings consistent with **head and neck mucosal squamous cell carcinoma** (HNSCC).

Although most head and neck cancers are linked to tobacco and excessive alcohol use, patients with **oropharyngeal carcinoma** (eg, tonsil, base of tongue) often **lack traditional risk factors**. Instead, oropharyngeal cancer is frequently associated with **human papillomavirus** (HPV) exposure, particularly in **younger** patients. HPV-positive HNSCC primarily affects the oropharynx, possibly due to the higher concentration of lymphatic tissue facilitating viral processing. The most common causative subtypes are **HPV-16 and 18**, which are covered by the HPV vaccine.

HPV is a nonenveloped, double-stranded DNA virus that infects cutaneous and mucosal tissues. Some strains (eg, HPV-1, HPV-2) cause skin warts. Others (eg, HPV-6, HPV-11) cause anogenital papillomas or papillomas that affect the upper respiratory tract (ie, recurrent respiratory papillomatosis). **High-risk strains** (eg, HPV-16, HPV-18) produce proteins **(E6, E7)** that prevent apoptosis, promote cellular proliferation, and cause genetic instability; they are also linked to cancer of the cervix, vulva, anus, and penis.

(Choice A) Coxsackievirus is the leading cause of hand-foot-and-mouth disease, which is characterized

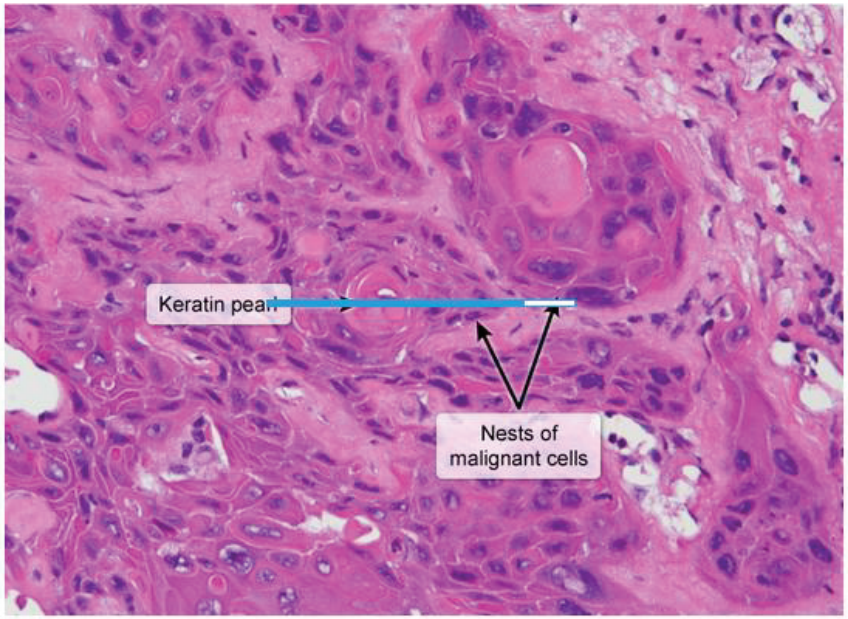
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Biopsy of the ulcerative tonsil lesion in this patient with persistent throat pain shows malignant cells with

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Keratinizing squamous cell carcinoma



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penis.

(Choice A) Coxsackievirus is the leading cause of hand-foot-and-mouth disease, which is characterized by low-grade fever, oral macules/vesicles, and a macular/papular/vesicular rash on the hands, feet, and extremities. This virus does not typically cause malignant transformation.

(Choice B) Epstein-Barr virus (EBV) can also cause HNSCC; however, it is most specifically implicated in the *nasopharynx*, rather than the oropharynx. The classic triad of nasopharyngeal carcinoma is a neck mass, nasal obstruction, and a unilateral, persistent middle ear effusion due to obstruction of the eustachian tube.

(Choice C) Herpes simplex virus causes latent infection in the sensory nerves. It is associated with vesicular lesions of the orolabial mucosa, not tonsillar ulcers, and does not cause HNSCC.

(Choice D) HIV increases the risk of many types of cancer due to immune dysregulation. The risk of cancers related to underlying infections, such as human herpesvirus 8 (Kaposi sarcoma), HPV, EBV, and hepatitis B and C viruses (hepatocellular carcinoma), is particularly increased. However, oropharyngeal cancer is most tightly linked to underlying HPV infection even in the setting of HIV.

Educational objective:

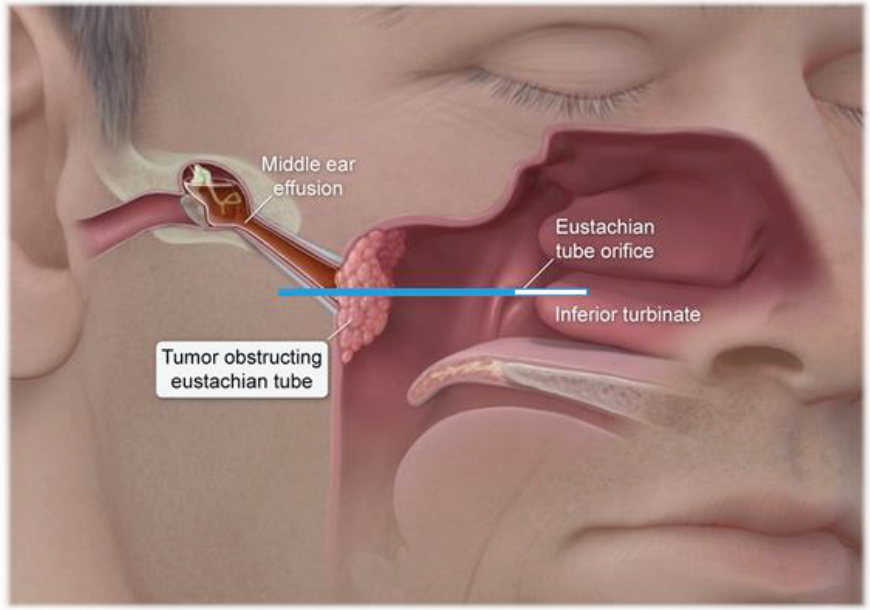
Most oropharyngeal carcinomas (eg, tonsil, base of tongue) are caused by human papilloma virus (HPV)

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Middle ear effusion due to nasopharyngeal carcinoma



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Most oropharyngeal carcinomas (eg, tonsil, base of tongue) are caused by human papilloma virus (HPV).

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eustachian tube.

(Choice C) Herpes simplex virus causes latent infection in the sensory nerves. It is associated with vesicular lesions of the orolabial mucosa, not tonsillar ulcers, and does not cause HNSCC.

(Choice D) HIV increases the risk of many types of cancer due to immune dysregulation. The risk of cancers related to underlying infections, such as human herpesvirus 8 (Kaposi sarcoma), HPV, EBV, and hepatitis B and C viruses (hepatocellular carcinoma), is particularly increased. However, oropharyngeal cancer is most tightly linked to underlying HPV infection even in the setting of HIV.

Educational objective:

Most oropharyngeal carcinomas (eg, tonsil, base of tongue) are caused by human papilloma virus (HPV) infection. HPV-16 and HPV-18 are particularly likely to cause malignant transformation.

References

- HPV associated head and neck cancer.

Microbiology	Infectious Diseases	Head and neck cancers
Subject	System	Topic

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A 12-year-old girl is brought to an urgent care clinic due to nausea, vomiting, and crampy abdominal pain 3 hours after a summer cookout in a park, where she consumed potato salad, coleslaw, and a hamburger. Two other children who attended the event also had similar symptoms. She has no chronic medical conditions and previously felt well. On examination, the patient is afebrile, and the abdomen is soft and nontender. Her symptoms quickly resolve with supportive care. Which of the following strategies would have been most effective in preventing this patient's illness?

A. Avoiding close contact with a person with similar symptoms
B. Cooking meat products to safe minimum temperatures
C. Keeping prepared foods refrigerated while storing
D. Performing adequate treatment of drinking water
E. Washing hands thoroughly before consuming a meal

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A 12-year-old girl is brought to an urgent care clinic due to nausea, vomiting, and crampy abdominal pain 3 hours after a summer cookout in a park, where she consumed potato salad, coleslaw, and a hamburger. Two other children who attended the event also had similar symptoms. She has no chronic medical conditions and previously felt well. On examination, the patient is afebrile, and the abdomen is soft and nontender. Her symptoms quickly resolve with supportive care. Which of the following strategies would have been most effective in preventing this patient's illness?

A. ~~Avoiding close contact with a person with similar symptoms~~ (0%)
B. Cooking meat products to safe minimum temperatures (12%)
C. Keeping prepared foods refrigerated while storing (82%)
D. Performing adequate treatment of drinking water (0%)
E. Washing hands thoroughly before consuming a meal (3%)

Correct

82% Answered correctly
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Enterotoxigenic *Staphylococcus aureus* produces a heat-stable enterotoxin that is a common cause of foodborne illness. This pathogen is typically introduced into high-risk foods (eg, mayonnaise-based salads, eggs, dairy, previously cooked meats) during improper food handling by an asymptomatic carrier. Storage at **room temperature** for extended periods allows the organism to quickly proliferate and generate enterotoxin. Individuals then ingest the **preformed enterotoxin** and become rapidly ill with nausea, **vomiting**, abdominal pain, and, occasionally, fever and mild diarrhea. Symptoms quickly resolve with supportive care. Multiple individuals are often affected due to the consumption of the same food at a picnic, party, or potluck.

Staphylococcal foodborne illness can be prevented by washing hands thoroughly with soap and water prior to preparing food (prevents contamination) and ensuring **proper refrigerated food storage** when food will not be consumed within 2 hours of preparation (prevents bacterial proliferation/enterotoxin production).

(Choice A) Close contact with an individual who has rotavirus infection can lead to the transmission of the virus with subsequent acute infectious diarrhea (particularly in young children [age <5]). Staphylococcal gastroenteritis occurs when a preformed toxin is ingested in food; person-to-person transmission does not occur.

(Choice B) Enterohemorrhagic *Escherichia coli* is typically transmitted due to eating undercooked,

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occur.

(Choice B) Enterohemorrhagic *Escherichia coli* is typically transmitted due to eating undercooked, contaminated ground beef. Manifestations typically begin 3-4 days (not hours) after ingestion and include toxin-mediated (Shiga toxin) colitis with bloody stools; some patients may also develop hemolytic uremic syndrome.

(Choice D) Treatment of drinking water can prevent giardia infection, which usually causes foul-smelling, watery diarrhea 7-10 days after transmission.

(Choice E) Washing hands prior to eating can prevent the transmission of a wide range of pathogens. Hand washing would not be protective against enterotoxins present in food.

Educational objective:
Staphylococcal foodborne illness is due to the consumption of a preformed enterotoxin in contaminated food. Most cases can be prevented by washing hands thoroughly prior to food preparation (prevents contamination) and ensuring proper refrigerated storage (prevents bacterial proliferation/enterotoxin production).

Microbiology Infectious Diseases Foodborne illness

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A 43-year-old man visiting the United States from Thailand comes to the emergency department due to 10 days of hemoptysis. He also has had night sweats but reports no fever or weight loss. Temperature is 37.7 C (99.9 F), blood pressure is 118/68 mm Hg, pulse is 86/min, and respirations are 18/min. Physical examination shows right-sided rhonchi and crackles. Chest x-ray shows an infiltrate in the right upper lobe. Sputum samples from 3 consecutive days are also obtained. After 72 hours of tuberculin skin test (TST) placement, there is no induration at the site; however, 2 of 3 sputum sample smears reveal acid-fast bacilli. Which of the following best explains the negative TST in this patient?

A. Childhood bacille Calmette-Guérin vaccination
B. Coexisting autoantibody disorder
C. Inadequate lymphocytic response
D. Inadequate time for dermal reaction
E. Nontuberculous mycobacterial infection

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A 43-year-old man visiting the United States from Thailand comes to the emergency department due to 10 days of hemoptysis. He also has had night sweats but reports no fever or weight loss. Temperature is 37.7 C (99.9 F), blood pressure is 118/68 mm Hg, pulse is 86/min, and respirations are 18/min. Physical examination shows right-sided rhonchi and crackles. Chest x-ray shows an infiltrate in the right upper lobe. Sputum samples from 3 consecutive days are also obtained. After 72 hours of tuberculin skin test (TST) placement, there is no induration at the site; however, 2 of 3 sputum sample smears reveal acid-fast bacilli. Which of the following best explains the negative TST in this patient?

A. Childhood bacille Calmette-Guérin vaccination (8%)
B. Coexisting autoantibody disorder (2%)
✓ C. Inadequate lymphocytic response (63%)
D. Inadequate time for dermal reaction (4%)
E. Nontuberculous mycobacterial infection (20%)

63% 01 min, 27 secs 01/08/2021

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This patient from Thailand has hemoptysis, night sweats, right upper lobe infiltrate, and positive sputum acid-fast bacillus stain, raising strong suspicion for **active pulmonary TB**. Tuberculin skin testing (**TST**) is generally positive in patients with active TB because differentiated lymphocytes recognize injected tuberculin antigens and trigger a strong type IV (cell-mediated) hypersensitivity response, leading to a large wheal of induration within 48-72 hours.

However, approximately 25% of patients with active TB have **false negative TST** (T cell **anergy**). In these individuals, an **impaired lymphocyte response** results in minimal or no induration after exposure to tuberculin antigens. Because a weak cell-mediated response increases the **risk of severe disseminated TB**, patients with active disease who have TST anergy are at much greater risk for TB-related morbidity and mortality.

A false-negative TST can also be seen with recent infection (it takes approximately 8 weeks for the cell mediated response to fully form), immunocompromise (eg, HIV), improper injection technique, and natural waning of immunity to latent infection. Because active TB requires a microbial diagnosis (eg, identifying the organism on sputum sample), neither TST nor interferon-gamma release assay can be used to diagnose or exclude the disease.

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(Choice A) Bacille Calmette-Guérin vaccination uses *Mycobacterium bovis*, which shares antigens with tuberculous mycobacteria. This vaccination primes the lymphocyte response against *Mycobacterium tuberculosis*, therefore protecting against infection, morbidity, and mortality. Patients with previous BCG vaccination can have false-positive (not false negative) TST.

(Choice B) TB infection is primarily controlled by macrophages and T lymphocytes. The humoral immune system plays a minimal role and does not contribute to TST induration. Therefore, an autoantibody disorder is unlikely to cause anergy.

(Choice D) Induration typically takes 48-72 hours to form following TST. This patient's test was negative at 72 hours, an appropriate time frame for TST interpretation.

(Choice E) Acid-fast bacillus stain and TST do not differentiate nontuberculous from tuberculous mycobacteria. Therefore, nontuberculous mycobacterial infection is a common cause of a false-positive (not a false-negative) TST. This patient's history of residence in a TB-endemic country, hemoptysis, night sweats, and upper lobe infiltrate are all highly suspicious for pulmonary TB.

Educational objective:
Approximately 25% of patients with active TB have false-negative tuberculin skin testing (TST) (anergy) due to an impaired cell-mediated immune response. These individuals are at greater risk for severe

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system plays a minimal role and does not contribute to TST induration. Therefore, an autoantibody disorder is unlikely to cause anergy.

(Choice D) Induration typically takes 48-72 hours to form following TST. This patient's test was negative at 72 hours, an appropriate time frame for TST interpretation.

(Choice E) Acid-fast bacillus stain and TST do not differentiate nontuberculous from tuberculous mycobacteria. Therefore, nontuberculous mycobacterial infection is a common cause of a false-positive (not a false-negative) TST. This patient's history of residence in a TB-endemic country, hemoptysis, night sweats, and upper lobe infiltrate are all highly suspicious for pulmonary TB.

Educational objective:

Approximately 25% of patients with active TB have false-negative tuberculin skin testing (TST) (anergy) due to an impaired cell-mediated immune response. These individuals are at greater risk for severe, disseminated disease and death. False-negative TST can also be seen with immunocompromise, improper injection technique, and recent infection.

References

- Tuberculin skin test result and risk of death among persons with active TB.

Immunology Infectious Diseases Tuberculosis

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A 45-year-old woman with advanced HIV infection has been receiving antiretroviral therapy for several years. When treatment was first initiated, the patient's viral load rapidly decreased to undetectable levels and her CD4+ cell count remained above 200/mm^3. However, recent HIV RNA levels have increased above the detection threshold. After undergoing drug resistance testing, she is started on an integrase inhibitor, and her viral load decreases precipitously. Which of the following steps of viral replication is most likely to be inhibited as a result of this patient's new treatment?

A. Cleavage of a viral polyprotein precursor
B. Complementary DNA synthesis from a viral RNA template
C. Fusion of viral and host phospholipid bilayers
D. Production of viral messenger RNA
E. Viral attachment to host cells

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A 45-year-old woman with advanced HIV infection has been receiving antiretroviral therapy for several years. When treatment was first initiated, the patient's viral load rapidly decreased to undetectable levels and her CD4+ cell count remained above 200/mm^3. However, recent HIV RNA levels have increased above the detection threshold. After undergoing drug resistance testing, she is started on an integrase inhibitor, and her viral load decreases precipitously. Which of the following steps of viral replication is most likely to be inhibited as a result of this patient's new treatment?

A. Cleavage of a viral polyprotein precursor (18%)
B. ~~Complementary DNA synthesis from a viral RNA template~~ (24%)
C. ~~Fusion of viral and host phospholipid bilayers~~ (12%)
✓ D. Production of viral messenger RNA (35%)
E. ~~Viral attachment to host cells~~ (7%)

Correct

35%
Answered correctly

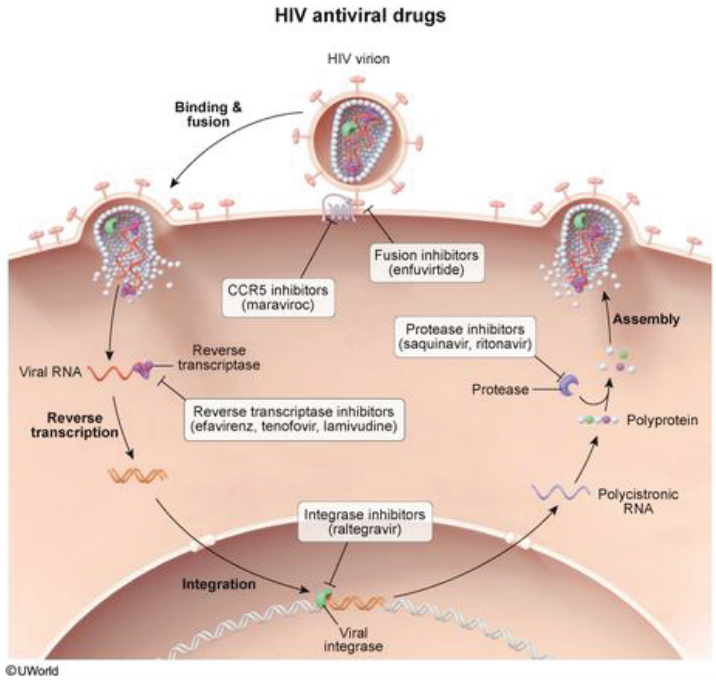
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After an HIV virion enters a host cell, viral RNA is released from the nucleocapsid and transcribed into **double-stranded DNA** by reverse transcriptase. The viral DNA then enters the nucleus and, through the actions of **integrase**, permanently **inserts into** the host cell's **chromosomes** to become a provirus. RNA polymerase II then transcribes viral mRNA from the proviral DNA. Once synthesized, HIV mRNA exits through the nuclear pores into the cytoplasm, where it uses the host cell's ribosomes to translate the enzymes, glycoproteins, structural proteins, and regulatory proteins needed to promote viral replication and transmission. The full-length mRNA also serves as the viral genome that is packaged into newly synthesized virions.

Raltegravir is an **integrase inhibitor** that disrupts the ability of double-stranded HIV DNA to integrate into the host cell's chromosomes. In the absence of integration, the **viral genome cannot be transcribed** by host cellular machinery and is eventually degraded by nucleases.

(Choice A) Most of the proteins necessary for HIV replication are translated into a polyprotein precursor that is then cleaved into individual proteins by viral and cellular protease enzymes. The action of viral protease can be directly prevented by protease inhibitors such as saquinavir.

(Choice B) Complementary DNA synthesis from the HIV RNA template is directly impaired by nucleoside

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protease can be directly prevented by protease inhibitors such as saquinavir.

(Choice B) Complementary DNA synthesis from the HIV RNA template is directly impaired by nucleoside and non-nucleoside reverse transcriptase inhibitors.

(Choice C) Drugs that bind to gp41, HIV's transmembrane envelope protein, are known as fusion inhibitors (eg, enfuvirtide). These drugs prevent gp41 from undergoing the conformational changes necessary for viral membrane fusion with the host cell membrane.

(Choice E) For HIV to infect a cell, the envelope glycoprotein gp120 must bind to both a CD4 molecule and a chemokine receptor (eg, CXCR4 or CCR5). CCR5 antagonists, such as maraviroc, exert their antiviral activity against HIV by blocking attachment and entry of CCR5-tropic viruses into CD4+ T cells and macrophages.

Educational objective:
Integration of double-stranded HIV DNA into the host cell's chromosomes is necessary to induce viral gene expression and prevent degradation of the viral genome. Raltegravir is an integrase inhibitor that disrupts HIV genome integration, preventing synthesis of viral mRNA.

References

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A 39-year-old paraplegic man with an indwelling bladder catheter comes to the emergency department complaining of 24 hours of rigors, nausea, and vomiting. His temperature is 38.9 C (102 F). Physical examination shows suprapubic and costovertebral angle tenderness. Urinalysis shows 3+ leukocyte esterase and numerous white blood cells. Urine and blood cultures grow non-lactose-fermenting Gram-negative rods. Which of the following pathogens is the most likely culprit?

A. *Enterobacter cloacae*
B. *Enterococcus faecalis*
C. *Escherichia coli*
D. *Klebsiella pneumoniae*
E. *Pseudomonas aeruginosa*
F. *Staphylococcus saprophyticus*

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A 39-year-old paraplegic man with an indwelling bladder catheter comes to the emergency department complaining of 24 hours of rigors, nausea, and vomiting. His temperature is 38.9 C (102 F). Physical examination shows suprapubic and costovertebral angle tenderness. Urinalysis shows 3+ leukocyte esterase and numerous white blood cells. Urine and blood cultures grow non-lactose-fermenting Gram-negative rods. Which of the following pathogens is the most likely culprit?

A. *Enterobacter cloacae* (4%)
B. ~~*Enterococcus faecalis*~~ (4%)
C. *Escherichia coli* (17%)
D. *Klebsiella pneumoniae* (9%)
E. *Pseudomonas aeruginosa* (61%)
F. ~~*Staphylococcus saprophyticus*~~ (2%)

Incorrect
Correct answer

61%
Answered correctly

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Patients with indwelling bladder catheters are at increased risk for urinary tract infections (UTIs) caused by both typical (eg, *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus saprophyticus*, *Proteus mirabilis*) and opportunistic (eg, *Pseudomonas*, *Enterococcus*, other Staphylococci, fungal) organisms. This patient's culture results are consistent with *Pseudomonas aeruginosa*, the only non-lactose-fermenting, Gram-negative rod listed. It is also the only one that is oxidase positive.

(Choice A) *Enterobacter cloacae* is a lactose-fermenting, Gram-negative rod characterized by extensive antibiotic resistance. It causes nosocomial infections, including UTIs, pneumonia, and surgical site infections.

(Choice B) *Enterococcus faecalis* is a Gram-positive coccus in the *Enterococcaceae* family that is a common cause of opportunistic UTIs. Vancomycin-resistant *Enterococcus* is a particularly fearsome isolate that is increasing in prevalence.

(Choice C) *Escherichia coli* is a lactose-fermenting, Gram-negative rod and the leading cause of both complicated (including catheter-associated) and uncomplicated UTIs.

(Choice D) *Klebsiella pneumoniae* is a lactose-fermenting, Gram-negative rod. It is a common cause of spontaneous bacterial peritonitis and nosocomial pneumonias as well as UTIs.

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that is increasing in prevalence.

(Choice C) *Escherichia coli* is a lactose-fermenting, Gram-negative rod and the leading cause of both complicated (including catheter-associated) and uncomplicated UTIs.

(Choice D) *Klebsiella pneumoniae* is a lactose-fermenting, Gram-negative rod. It is a common cause of spontaneous bacterial peritonitis and nosocomial pneumonias as well as UTIs.

(Choice F) *Staphylococcus saprophyticus* is a catalase-positive, coagulase-negative, Gram-positive coccus that typically causes UTIs in sexually active women. It is differentiated from *S epidermidis* by being novobiocin resistant.

Educational objective:
Pseudomonas aeruginosa is an oxidase-positive, non-lactose-fermenting, Gram-negative organism. It is a common cause of urinary tract infections in patients with indwelling bladder catheters.

Microbiology	Infectious Diseases	Urinary tract infection
Subject	System	Topic

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A 72-year-old man is brought to the emergency department from a skilled nursing facility due to altered mental status, skin flushing, and a high fever. His temperature is 38.9 C (102 F), blood pressure is 80/40 mm Hg, pulse is 120/min, and respirations are 26/min. If blood cultures are positive for *Escherichia coli*, which of the following is the most likely site of infection leading to bacteremia in this patient?

- A. Biliary tree
- B. Colon
- C. Lungs
- D. Oropharynx
- E. Skin
- F. Small intestine
- G. Urinary tract

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A 72-year-old man is brought to the emergency department from a skilled nursing facility due to altered mental status, skin flushing, and a high fever. His temperature is 38.9 C (102 F), blood pressure is 80/40 mm Hg, pulse is 120/min, and respirations are 26/min. If blood cultures are positive for *Escherichia coli*, which of the following is the most likely site of infection leading to bacteremia in this patient?

A. Biliary tree (1%)
B. Colon (6%)
C. Lungs (1%)
D. Oropharynx (1%)
E. Skin (0%)
F. Small intestine (4%)
G. Urinary tract (83%)

Correct
83%
29 secs
02/12/2021

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This elderly patient with fever, hypotension, altered mental status, and *Escherichia coli* bacteremia has septic shock most likely due to **urinary tract infection (UTI)**. UTIs are a common cause of sudden disorientation or confusion in the elderly. Predisposing factors include urinary obstruction (eg, benign prostatic hypertrophy), fecal incontinence, neurogenic bladder (eg, due to diabetes), and frequent or indwelling catheterization. *E coli* is the most common organism causing UTI (others are *Proteus, Klebsiella, Enterobacter, Citrobacter*, and *Pseudomonas*), and UTIs represent the most common cause of ***E coli* bacteremia**. *E coli* is part of the normal gastrointestinal (GI) flora. Some strains have adhesive fimbriae allowing them to potentially contaminate the urethra and ascend the urinary tract, leading to UTI or pyelonephritis.

Gram-negative sepsis or septic shock can ensue as a result of the body's systemic reaction to lipopolysaccharide endotoxin (a component in some gram-negative bacterial membranes). Signs of **sepsis** include hyper- or hypothermia, tachycardia, tachypnea (can lead to respiratory alkalosis), and leukocytosis. Severe sepsis is marked by **organ dysfunction** due to poor blood flow (eg, oliguria from poor renal perfusion and altered mental status from poor cerebral perfusion). Metabolic lactic acidosis can be seen, particularly during the late stages, due to poor tissue perfusion. Treatment is focused on maintaining blood pressure and organ perfusion with intravenous fluids, administering antibiotics directed

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maintaining blood pressure and organ perfusion with intravenous fluids, administering antibiotics directed against the offending organism, and maintaining proper ventilation and oxygenation.

(Choice A) The biliary tree has many protective mechanisms against bacterial colonization and infection. The sphincter of Oddi prevents reflux of nonsterile duodenal contents into the biliary tree, bile salts can inhibit bacterial growth, downstream biliary flow helps to wash organisms away from the biliary tree, and bile secretory IgA helps to prevent bacterial adherence. Despite this, organisms such as *E coli, Klebsiella, Enterobacter*, and enterococci occasionally infect the biliary tract, leading to cholangitis that can cause sepsis if left untreated. However, this process is a much less frequent cause of bacteremia than UTI, and cholangitis classically presents with fever, abdominal pain, and jaundice.

(Choices B and F) Many microorganisms inhabit the human GI tract as normal flora. Under normal circumstances, small intestine bacteria do not cause systemic disease. Anaerobic or gram-negative rod bacteremia can result from colonic perforation due to surgery, trauma, or wall rupture from certain pathologic processes. However, the likely site of infection in this patient with *E coli* bacteremia is the genitourinary tract; although it may represent the ultimate site of origin of *E coli*, the GI tract is not typically a site of infection.

(Choices C and D) Bacterial causes of upper respiratory tract infection (eg, *Moraxella* and *Haemophilus*) do not usually cause disseminated disease. *E coli* and other gram-negative rods (*Pseudomonas,*

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a site of infection.

(Choices C and D) Bacterial causes of upper respiratory tract infection (eg, *Moraxella* and *Haemophilus*) do not usually cause disseminated disease. *E coli* and other gram-negative rods (*Pseudomonas, Acinetobacter*, and *Klebsiella*) would be common causes of health care-acquired pneumonia in this nursing home resident; from the lungs, these organisms can easily gain access to the bloodstream and cause sepsis. However, this patient does not have any respiratory symptoms, and *E coli* sepsis is more commonly due to UTI than pneumonia.

(Choice E) Normal skin flora includes mostly gram-positive organisms such as staphylococci and streptococci.

Educational objective:

Escherichia coli is the most common cause of urinary tract infection (UTI) in both healthy adults and elderly patients. *E coli* is a part of the normal gastrointestinal flora, and special adhesive proteins (fimbriae) allow some strains to colonize and ascend the urinary tract. This can result in UTI, pyelonephritis, or bacteremia and sepsis following access to the bloodstream. UTIs are the most common cause of *E coli* bacteremia.

Microbiology	Infectious Diseases	Urinary tract infection
Subject	System	Topic

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A 34-year-old man comes to the office due to a painless penile ulcer, which he first noticed 3 days ago. He had unprotected sexual intercourse with a new partner a few weeks ago. The patient has no significant medical history and takes no medications. Temperature is 37.1 C (98.8 F). Examination reveals a 2-cm nontender ulcer close to the glans penis with a raised, indurated margin and a clean base. There are no surrounding lesions or vesicles. There are several bilateral enlarged inguinal lymph nodes, which are firm, nontender, and rubbery. Physical examination is otherwise unremarkable. Rapid plasma reagin and HIV testing are negative. Infection with which of the following is the most likely cause of this patient's symptoms?

A. *Chlamydia trachomatis* (L serovars)
B. *Haemophilus ducreyi*
C. Herpes simplex virus
D. *Neisseria gonorrhoeae*
E. *Treponema pallidum*

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had unprotected sexual intercourse with a new partner a few weeks ago. The patient has no significant medical history and takes no medications. Temperature is 37.1 C (98.8 F). Examination reveals a 2-cm nontender ulcer close to the glans penis with a raised, indurated margin and a clean base. There are no surrounding lesions or vesicles. There are several bilateral enlarged inguinal lymph nodes, which are firm, nontender, and rubbery. Physical examination is otherwise unremarkable. Rapid plasma reagin and HIV testing are negative. Infection with which of the following is the most likely cause of this patient's symptoms?

A. *Chlamydia trachomatis* (L serovars) (28%)

B. *Haemophilus ducreyi* (6%)

C. Herpes simplex virus (3%)

D. *Neisseria gonorrhoeae* (1%)

✓ E. *Treponema pallidum* (59%)

Correct

59%

48 secs

02/10/2021

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Genital ulcer disease				
	Syphilis	**Genital herpes**	**Chancroid**	**Granuloma inguinale (donovanosis)**
Causative agent	*Treponema pallidum*	Herpes simplex virus	*Haemophilus ducreyi*	*Klebsiella granulomatis*
Description	Single, **painless** ulcer at inoculation site with heaped-up borders & clean base	Multiple, **painful superficial vesicles** or **ulcerations** with erythematous base	**Deep**, **purulent**, painful ulcers with matted/**suppurative** lymphadenitis	**Painless**, progressive, red serpiginous ulcerative lesions **without** lymphadenopathy
				• Gram stain &

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	borders & clean base			lymphadenopathy
Diagnostic tests	• VDRL/RPR • Dark-field microscopy	• PCR • Tzanck smear	• Gram stain & culture • PCR	• Gram stain & culture (difficult) • Biopsy (Donovan bodies)

PCR = polymerase chain reaction; **RPR** = rapid plasma reagin; **VDRL** = Venereal Disease Research Laboratory.

This patient developed a **genital ulcer** a few weeks after unprotected intercourse, raising suspicion for a sexually transmitted infection. A wide range of pathogens can cause genital ulcers, but a **solitary**, **painless ulcer** with heaped-up borders and a clean base usually indicates **primary syphilis** (syphilitic chancre). Syphilis is caused by ***Treponema pallidum***, a gram-negative spirochete that cannot be cultured and cannot be detected on Gram stain due to its small size.

The diagnosis of syphilis relies primarily on nontreponemal (eg, rapid plasma reagin, VDRL) and treponemal (eg, fluorescent treponemal antibody absorption) serologic testing. However, because humoral

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The diagnosis of syphilis relies primarily on nontreponemal (eg, rapid plasma reagin, VDRL) and treponemal (eg, fluorescent treponemal antibody absorption) serologic testing. However, because humoral antibody response often takes 4 weeks to develop, **false-negative serologic testing** is common early in the course of disease. Nontreponemal tests are particularly susceptible to initial false-negative results (as in this patient); treponemal tests are more sensitive in early infection and are often used preferentially in this setting.

Although not widely available, the diagnostic gold standard for syphilis is to directly visualize the organism in tissue scrapings from a cutaneous lesion (eg, chancre). This can involve fluorescent antibody testing or **dark-field microscopy**, which will show **motile**, **helical spirochetes**.

(Choice A) L serovars of *Chlamydia trachomatis* cause lymphogranuloma venereum. Although initial infection is associated with a painless genital ulcer, patients primarily present after the disease has spread to the regional lymph nodes, which results in painful lymphadenitis. This disease is very rare in the United States and occurs mostly in tropical and subtropical regions.

(Choice B) *Haemophilus ducreyi* is a small gram-negative rod that causes chancroid, a sexually transmitted infection characterized by painful (not painless) genital ulcers with an erythematous base. Lesions typically begin as papules or pustules and evolve into an ulcer. More than one lesion is often

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(Choice B) *Haemophilus ducreyi* is a small gram-negative rod that causes chancroid, a sexually transmitted infection characterized by painful (not painless) genital ulcers with an erythematous base. Lesions typically begin as papules or pustules and evolve into an ulcer. More than one lesion is often present.

(Choice C) Herpes simplex virus usually causes multiple, bilateral, painful, ulcerating lesions. Initial infections are frequently associated with systemic symptoms (eg, fever, headache, myalgia) and tender lymphadenopathy.

(Choice D) *Neisseria gonorrhoeae*, a gram-negative diplococcus, is a leading cause of cervicitis, urethritis, and pelvic inflammatory disease. Infected patients usually have copious purulent discharge from the urethra; ulcerative genital lesions are not a feature of this organism.

Educational objective:
Patients with early syphilis (eg, chancre) often have false-negative initial serologic testing. Direct visualization of the organism (*Treponema pallidum*) by dark-field microscopy or fluorescent antibody testing is the gold standard for diagnosis but is not widely available.

Microbiology | Infectious Diseases | Syphilis

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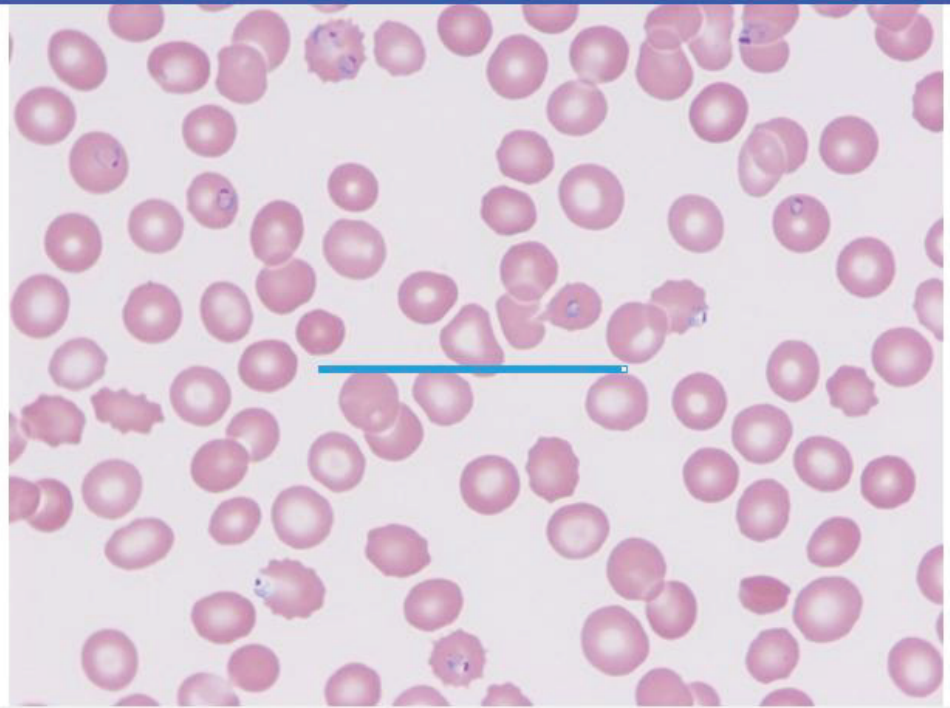
A 24-year-old woman comes to the emergency department due to 2 days of fever. The patient has no chronic medical conditions, drinks alcohol occasionally, and does not use tobacco or illicit drugs. She is sexually active and frequently travels for her work as a freelance journalist. Temperature is 38.3 C (101 F), blood pressure is 118/66 mm Hg, pulse is 106/min, and respirations are 18/min. Physical examination is notable for mild scleral icterus and splenomegaly. Laboratory findings are shown in the exhibit. Which of the following infectious agents is most likely responsible for this patient's current condition?

A. *Borrelia burgdorferi*
B. *Leishmania tropica*
C. *Plasmodium falciparum*
D. *Schistosoma mansoni*
E. *Toxocara canis*
F. *Trichinella spiralis*
G. *Wuchereria bancrofti*

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Exhibit Display



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chronic medical conditions, drinks alcohol occasionally, and does not use tobacco or illicit drugs. She is sexually active and frequently travels for her work as a freelance journalist. Temperature is 38.3 C (101 F), blood pressure is 118/66 mm Hg, pulse is 106/min, and respirations are 18/min. Physical examination is notable for mild scleral icterus and splenomegaly. Laboratory findings are shown in the exhibit. Which of the following infectious agents is most likely responsible for this patient's current condition?

- A. *Borrelia burgdorferi* (4%)
- B. *Leishmania tropica* (3%)
- ✓ C. *Plasmodium falciparum* (85%)
- D. *Schistosoma mansoni* (4%)
- E. *Toxocara canis* (0%)
- F. *Trichinella spiralis* (1%)
- G. *Wuchereria bancrofti* (0%)

Correct

85%

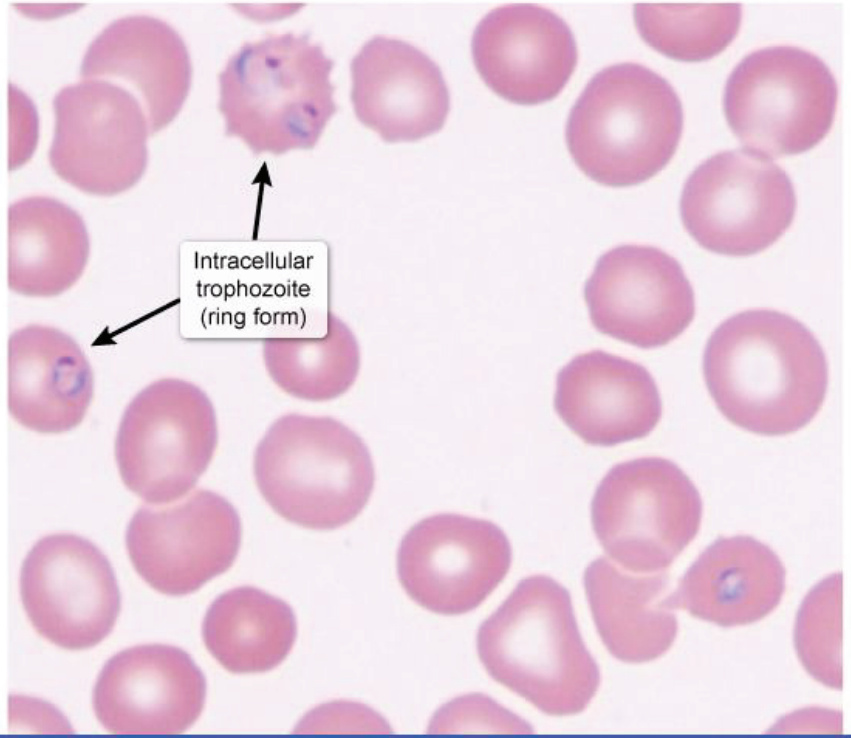
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Plasmodium falciparum



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This patient with fever, icterus, splenomegaly, and ring-shaped parasites within red blood cells has **malaria**, which is caused by 4 main species of ***Plasmodium*** (*P falciparum*, *P vivax*, *P ovale*, *P knowlesi*). Although malaria has been eradicated from the United States, cases still arise due to travel to endemic regions, particularly when no chemoprophylaxis is taken.

The parasite is transmitted by female *Anopheles* mosquitos during blood feeding, travels to the liver where it infects hepatocytes, and then subsequently undergoes asexual reproduction, which generates hepatic schizonts with thousands of daughter cells (merozoites). Rupture of the schizont into the circulatory system leads to erythrocyte infection and cycles of intraerythrocytic reproduction.

As the parasite disseminates throughout the circulation, production of inflammatory cytokines causes nonspecific symptoms (eg, fatigue, fever, malaise, headache) and, sometimes, life-threatening complications (eg, seizure, renal failure, circulatory collapse). Hepatosplenomegaly and signs of anemia and hyperbilirubinemia (eg, scleral icterus) are often present. The diagnosis is confirmed when peripheral blood microscopy shows **intraerythrocytic** trophozoites with a **"diamond ring" appearance**.

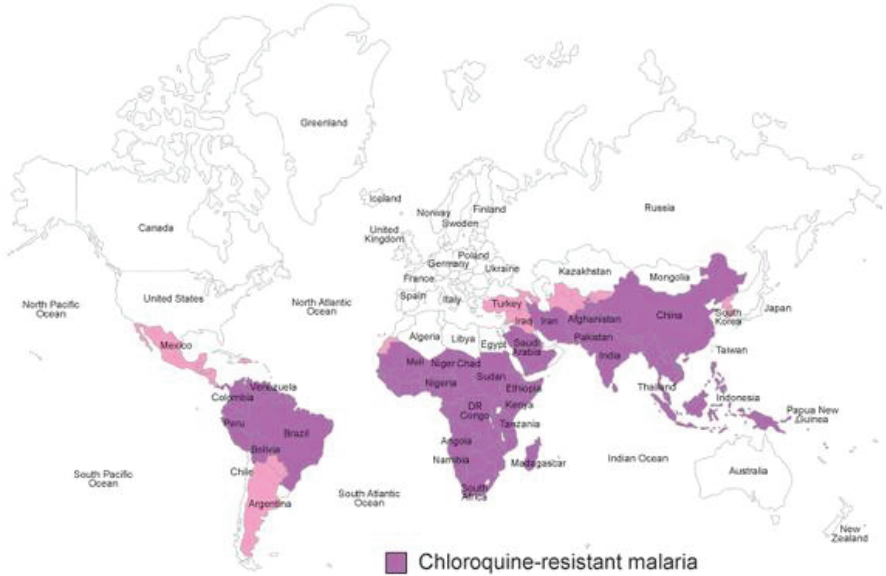
(Choice A) *Borrelia burgdorferi*, the causative organism of Lyme disease, is a spirochete transmitted by the *Ixodes* tick. It cannot be visualized by conventional light microscopy; diagnosis is made based on clinical symptoms and/or serology.

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Exhibit Display

Map of malaria regions



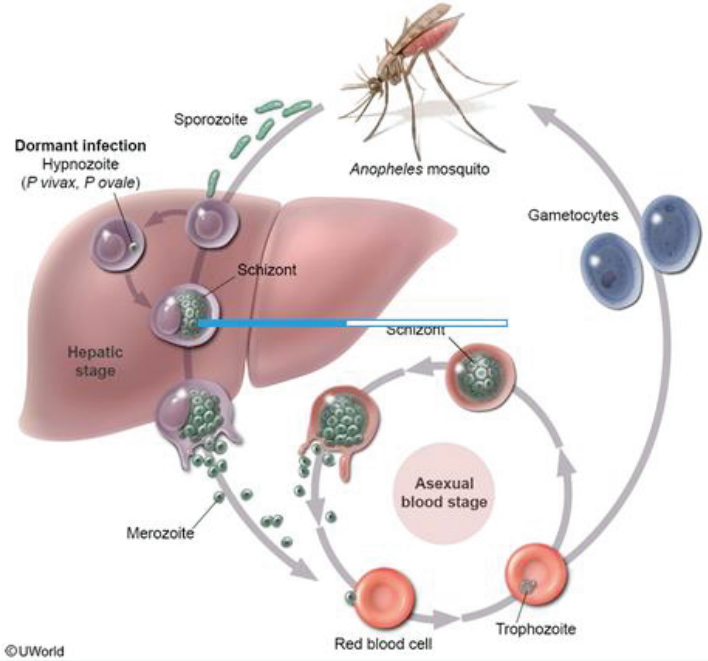
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clinical symptoms and/or serology.

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Exhibit Display

Malaria life cycle



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clinical symptoms and/or serology.

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clinical symptoms and/or serology.

(Choice B) *Leishmania tropica*, a protozoa transmitted by sandflies, causes a papule at the site of inoculation that evolves over weeks or years into an ulcer with an indurated border. Microscopy can show the oval-round organism within white blood cells.

(Choice D) *Schistosoma mansoni* is a parasitic blood fluke transmitted when humans swim in fresh water contaminated with infected snails. Schistosomes mature in the liver, reside in the mesenteric venules, and release eggs that can cause chronic eosinophilic granulomatous inflammation/fibrosis in organs (eg, bladder, liver, spleen, gastrointestinal tract). Diagnosis is made by identifying eggs in urine or stool, or on biopsy.

(Choice E) *Toxocara canis*, also known as dog roundworm, incidentally infects humans and causes eosinophilic granulomatous inflammation in organs (visceral larva migrans) or the eye (ocular larva migrans). Diagnosis is made by serology.

(Choice F) *Trichinella spiralis* is a roundworm infection that can be transmitted to humans when they ingest larvae (eg, from contaminated pork). Larvae spread through the blood to the muscle and form cysts, causing muscle pain, weakness, and swelling. Diagnosis is usually made by serology or muscle biopsy; the parasite is not intraerythrocytic.

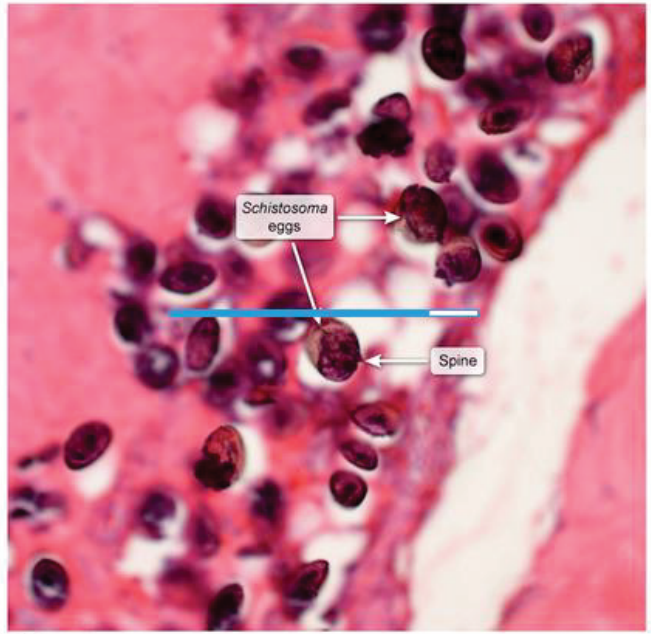
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clinical symptoms and/or serology

Exhibit Display

Schistosomiasis



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(Choice E) *Toxocara canis*, also known as dog roundworm, incidentally infects humans and causes eosinophilic granulomatous inflammation in organs (visceral larva migrans) or the eye (ocular larva migrans). Diagnosis is made by serology.

(Choice F) *Trichinella spiralis* is a roundworm infection that can be transmitted to humans when they ingest larvae (eg, from contaminated pork). Larvae spread through the blood to the muscle and form cysts, causing muscle pain, weakness, and swelling. Diagnosis is usually made by serology or muscle biopsy; the parasite is not intraerythrocytic.

(Choice G) *Wuchereria bancrofti* is a roundworm that is transmitted by mosquitos and causes lymphatic infection (eg, lymphedema, adenolymphangitis). Blood smear (performed in the evening) can often demonstrate the long, thin microfilaria in the circulation; it is not ring-shaped or intraerythrocytic.

Educational objective:
Malaria is diagnosed when intraerythrocytic diamond ring–shaped parasites are seen on peripheral blood smear. This disease should be suspected in travelers to endemic regions who develop a febrile illness.

Microbiology	Infectious Diseases	Malaria
Subject	System	Topic

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A 35-year-old homeless man comes to the emergency department due to urinary urgency, burning sensation on urination, and urethral discharge. The patient had similar symptoms 3 months ago, and urethral swab microscopy revealed numerous neutrophils and gram-negative diplococci. The symptoms resolved after treatment with ceftriaxone and azithromycin but recurred 4 days ago. The patient was advised to use condoms but has had many unprotected sexual encounters recently. He has no other medical problems. The patient occasionally drinks alcohol and smokes cigarettes. Temperature is 37.1 C (98.8 F). BMI is 18.8 kg/m^2. No suprapubic or flank tenderness is present on examination. Mild erythema is noted at the urethral meatus. Nucleic acid amplification testing of a clean catch urine specimen is positive for *Neisseria gonorrhoeae*. Which of the following is the most likely reason for the recurrence of infection in this patient?

A. Complete absence of memory T cells
B. Decreased antibody production due to malnutrition
C. High variability of microbial antigenic structure
D. Poor antigen recognition due to antigenic mimicry
E. Resistance to antimicrobial agents

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resolved after treatment with ceftriaxone and azithromycin but recurred 4 days ago. The patient was advised to use condoms but has had many unprotected sexual encounters recently. He has no other medical problems. The patient occasionally drinks alcohol and smokes cigarettes. Temperature is 37.1 C (98.8 F). BMI is 18.8 kg/m^2. No suprapubic or flank tenderness is present on examination. Mild erythema is noted at the urethral meatus. Nucleic acid amplification testing of a clean catch urine specimen is positive for *Neisseria gonorrhoeae*. Which of the following is the most likely reason for the recurrence of infection in this patient?

A. Complete absence of memory T cells
B. Decreased antibody production due to malnutrition
C. High variability of microbial antigenic structure
D. Poor antigen recognition due to antigenic mimicry
E. Resistance to antimicrobial agents

Submit

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resolved after treatment with ceftriaxone and azithromycin but recurred 4 days ago. The patient was advised to use condoms but has had many unprotected sexual encounters recently. He has no other medical problems. The patient occasionally drinks alcohol and smokes cigarettes. Temperature is 37.1 C (98.8 F). BMI is 18.8 kg/m^2. No suprapubic or flank tenderness is present on examination. Mild erythema is noted at the urethral meatus. Nucleic acid amplification testing of a clean catch urine specimen is positive for *Neisseria gonorrhoeae*. Which of the following is the most likely reason for the recurrence of infection in this patient?

A. Complete absence of memory T cells (2%)

B. Decreased antibody production due to malnutrition (6%)

✓ C. High variability of microbial antigenic structure (80%)

D. Poor antigen recognition due to antigenic mimicry (3%)

E. Resistance to antimicrobial agents (6%)

Correct

80%

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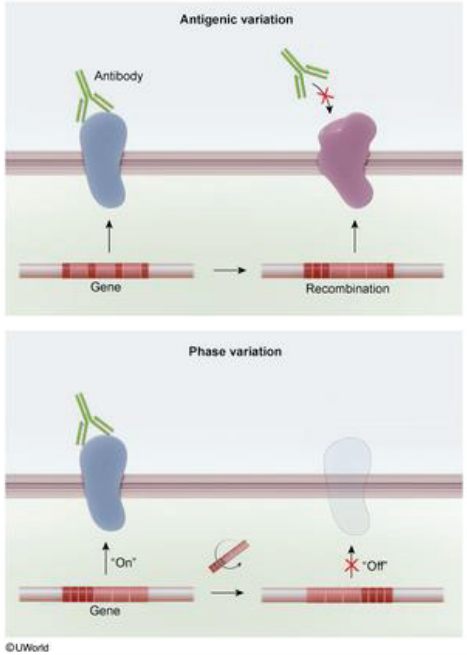
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Exhibit Display

Bacterial mechanisms for immune evasion



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This patient's symptoms of **gonococcal urethritis** (dysuria, urinary discharge) resolved with ceftriaxone and then recurred several months later after unprotected sexual encounters, raising suspicion for reinfection. Although infection with *Neisseria gonorrhoeae* does lead to the formation of IgA and IgG antibodies, the **high variability of gonococcal surface antigens** (eg, porins, Opa proteins, lipooligosaccharide) limits the effectiveness of the antibody response. As such, previous infection with *N gonorrhoeae* results in almost **no protective immunity** against future infections.

(Choice A) Memory T cells form in response to gonococcal infection but are not effective at preventing reinfection due to high antigenic variation (which prevents recognition of the organism).

(Choice B) The humoral antibody response can be impaired by severe malnutrition; however, the high rate of antigenic variability in gonococcal infection would already preclude development of an effective antibody response.

(Choice D) Antigenic mimicry occurs when an organism displays similar antigens to the host, preventing the host's immune system from recognizing the organism as foreign.

(Choice E) Gonorrhea is largely susceptible to third-generation cephalosporins (eg, ceftriaxone) but may be resistant to penicillins, macrolides, and fluoroquinolones. Antibiotic resistance should be suspected when initial symptoms do not improve with treatment. Because this patient's initial symptoms resolved after

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(Choice D) Antigenic mimicry occurs when an organism displays similar antigens to the host, preventing the host's immune system from recognizing the organism as foreign.

(Choice E) Gonorrhea is largely susceptible to third-generation cephalosporins (eg, ceftriaxone) but may be resistant to penicillins, macrolides, and fluoroquinolones. Antibiotic resistance should be suspected when initial symptoms do not improve with treatment. Because this patient's initial symptoms resolved after being treated with ceftriaxone and then recurred several months later, reinfection is far more likely than drug resistance. Patients with gonorrhea infection are also treated with azithromycin or doxycycline for potential *Chlamydia trachomatis* coinfection (which occurs in ~30% of patients).

Educational objective:

Neisseria gonorrhoeae has high antigenic variability of its surface molecules (eg, porins, Opa proteins), which prevents the formation of protective immunity and leads to susceptibility to repeat infection.

References

- New concepts in immunity to Neisseria Gonorrhoeae: innate responses and suppression of adaptive immunity favor the pathogen, not the host.

Microbiology	Infectious Diseases	Urethritis
Subject	System	Topic

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A 65-year-old woman with ovarian cancer undergoing chemotherapy is hospitalized due to fever, headache, ataxia, and progressive confusion. Two days later, a 26-year-old pregnant woman is admitted to the same hospital with fever, nausea, vomiting, diarrhea, and muscle aches and spontaneously delivers a preterm infant who has generalized skin rash. Laboratory evaluation reveals that these patients' conditions were caused by the same microbial organism. The state health department is notified. Reports of similar illnesses are noted in neighboring cities. A subsequent investigation reveals that 8 people were affected, all of whom consumed food products from a single processing facility. Which of the following organisms is most likely responsible for this outbreak?

- A. *Aspergillus fumigatus*
- B. Cytomegalovirus
- C. *Escherichia coli* O157:H7
- D. Herpes simplex virus
- E. *Listeria monocytogenes*
- F. *Neisseria meningitidis*

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illnesses are noted in neighboring cities. A subsequent investigation reveals that 8 people were affected, all of whom consumed food products from a single processing facility. Which of the following organisms is most likely responsible for this outbreak?

A. *Aspergillus fumigatus*
B. Cytomegalovirus
C. *Escherichia coli* O157:H7
D. Herpes simplex virus
E. *Listeria monocytogenes*
F. *Neisseria meningitidis*
G. *Streptococcus pneumoniae*
H. *Toxoplasma gondii*

Submit

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illnesses are noted in neighboring cities. A subsequent investigation reveals that 8 people were affected, all of whom consumed food products from a single processing facility. Which of the following organisms is most likely responsible for this outbreak?

A. *Aspergillus fumigatus* (0%)
B. Cytomegalovirus (4%)
C. *Escherichia coli* O157:H7 (6%)
D. Herpes simplex virus (0%)
✓ E. *Listeria monocytogenes* (74%)
F. *Neisseria meningitidis* (0%)
G. *Streptococcus pneumoniae* (0%)
H. *Toxoplasma gondii* (12%)

Correct

74%
Answered correctly

55 secs
Time Spent

03/18/2021
Last Updated

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Listeria monocytogenes is a facultative intracellular gram-positive bacillus that can multiply at **refrigerated temperatures** in both anaerobic and microaerophilic conditions. It is an important cause of foodborne illness; outbreaks are frequently associated with consumption of **contaminated food products** (eg, processed meats, soft cheeses, raw fruits & vegetables).

Healthy patients who ingest high inoculums of *Listeria* are at risk for febrile **gastroenteritis**. Invasive infections such as sepsis and **meningoencephalitis** are primarily seen in patients with **impaired cell-mediated immunity** (eg, AIDS, malignancy, extremes of age, pregnancy). Pregnant women are at greatest risk in the third trimester and often present with flu-like symptoms and diarrhea. Infection during pregnancy can cause **preterm labor**, neonatal sepsis, or granulomatosis infantiseptica (ie, infant with papular & pustular skin lesions, widespread abscesses/granulomas).

(Choice A) Epidemic fungal meningitis due to *Aspergillus fumigatus* has been associated with contaminated glucocorticoid injections. *Aspergillus* is not typically associated with foodborne illness.

(Choices B and D) Cytomegalovirus and herpes simplex virus can cause a variety of clinical syndromes in immunocompromised patients, including encephalitis, esophagitis, pneumonitis, and colitis. These viruses are ubiquitous and not associated with foodborne outbreaks.

(Choice C) Foodborne outbreaks of *Escherichia coli* O157:H7 have been linked to the ingestion of

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(Choice C) Foodborne outbreaks of *Escherichia coli* O157:H7 have been linked to the ingestion of contaminated beef (primarily) and are usually associated with hemorrhagic colitis. Patients may also develop hemolytic uremic syndrome. Meningitis and neonatal infection would be atypical.

(Choice F) *Neisseria meningitidis* causes sepsis and acute meningitis. It is transmitted primarily by respiratory droplets; most cases occur in those who live in congregate settings (eg, dormitories, military barracks).

(Choice G) *Streptococcus pneumoniae* is a common cause of bacterial meningitis in elderly and immunocompromised individuals but is not associated with foodborne outbreaks.

(Choice H) *Toxoplasma* may be acquired via consumption of undercooked meat and unwashed produce or contact with cat feces. It is associated with meningoencephalitis in immunocompromised patients (eg, advanced AIDS). In immunocompetent individuals, toxoplasmosis is usually asymptomatic but may present with flu-like symptoms and lymphadenopathy; diarrhea would be less likely.

Educational objective:
Listeria is a relatively common foodborne illness associated with outbreaks after the consumption of contaminated food, particularly processed meats and dairy products. Healthy patients may develop gastroenteritis; patients with impaired cell-mediated immunity are at risk for invasive infection (eg, sepsis,

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respiratory droplets; most cases occur in those who live in congregate settings (eg, dormitories, military barracks).

(Choice G) *Streptococcus pneumoniae* is a common cause of bacterial meningitis in elderly and immunocompromised individuals but is not associated with foodborne outbreaks.

(Choice H) *Toxoplasma* may be acquired via consumption of undercooked meat and unwashed produce or contact with cat feces. It is associated with meningoencephalitis in immunocompromised patients (eg, advanced AIDS). In immunocompetent individuals, toxoplasmosis is usually asymptomatic but may present with flu-like symptoms and lymphadenopathy; diarrhea would be less likely.

Educational objective:
Listeria is a relatively common foodborne illness associated with outbreaks after the consumption of contaminated food, particularly processed meats and dairy products. Healthy patients may develop gastroenteritis; patients with impaired cell-mediated immunity are at risk for invasive infection (eg, sepsis, meningoencephalitis); and listeriosis in pregnancy is associated with adverse fetal outcomes (eg, fetal death, premature birth).

Microbiology Infectious Diseases Meningitis

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A 29-year-old male is hospitalized with low-grade fever and high serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST). His serum is positive for HBsAg. You should inform the patient that the most likely outcome for his infection would be:

A. Complete resolution

B. Fulminant hepatitis

C. Stable chronic hepatitis

D. Chronic hepatitis with progression to cirrhosis

E. Chronic hepatitis with progression to hepatocellular carcinoma

Submit

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A 29-year-old male is hospitalized with low-grade fever and high serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST). His serum is positive for HBsAg. You should inform the patient that the most likely outcome for his infection would be:

- A. Complete resolution (58%) ✓
- B. Fulminant hepatitis (5%)
- C. Stable chronic hepatitis (19%)
- D. Chronic hepatitis with progression to cirrhosis (9%)
- E. Chronic hepatitis with progression to hepatocellular carcinoma (7%)

Correct

58% Answered correctly

22 secs Time Spent

01/30/2021 Last Updated

Explanation

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Hepatitis B virus infection can produce one of three syndromes: acute hepatitis with complete resolution; chronic hepatitis (with or without cirrhosis and the attendant increased risk of hepatocellular carcinoma); or fulminant hepatitis with massive liver necrosis. By far the most common outcome in HBV-infected adults (> 95%) is acute hepatitis with mild or subclinical symptoms that eventually completely resolve.

(Choice B) Fulminant hepatitis occurs in < 1% of patients who develop acute hepatitis.

(Choice C) Only 4-5% of patients with hepatitis B virus infection will go on to develop chronic hepatitis. Of those, 50-80% will remain stable with no evidence of cirrhosis.

(Choice D) Approximately 20-50% of patients with chronic hepatitis B infection will also eventually develop cirrhosis.

(Choice E) Hepatocellular carcinoma arises in 10% of patients with chronic hepatitis and cirrhosis.

Educational Objective:
The most common outcome in HBV-infected adults (> 95%) is acute hepatitis with mild or subclinical symptoms that eventually completely resolve.

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A microbiologist is studying the structure and function of bacterial cell walls. In an experiment, group A streptococci are treated with chemicals to solubilize the cell wall. Various cell wall–associated proteins are subsequently extracted. Electron microscopic evaluation of a specific protein shows structural homology with mammalian tropomyosin and myosin. This protein acts as a virulence factor for certain species of the organism. Which of the following is the most likely function of this bacterial cell wall–associated protein?

A. Excrete antibiotics
B. Protect from osmotic lysis
C. Provide mechanical cell support
D. Resist phagocytosis
E. Transport nutrients into the cell

Submit

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A microbiologist is studying the structure and function of bacterial cell walls. In an experiment, group A streptococci are treated with chemicals to solubilize the cell wall. Various cell wall–associated proteins are subsequently extracted. Electron microscopic evaluation of a specific protein shows structural homology with mammalian tropomyosin and myosin. This protein acts as a virulence factor for certain species of the organism. Which of the following is the most likely function of this bacterial cell wall–associated protein?

A. ~~Excrete antibiotics~~ (5%)

B. ~~Protect from osmotic lysis~~ (7%)

C. Provide mechanical cell support (31%)

D. Resist phagocytosis (46%)

E. Transport nutrients into the cell (8%)

Incorrect
Correct answer
D

46%
Answered correctly

58 secs
Time Spent

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Gram-positive organisms have cell walls composed primarily of a thick peptidoglycan layer and teichoic acid. However, additional cell wall components are often present that contribute to virulence, motility, or the ability to adhere to epithelial surfaces. For instance, the cell wall of **group A streptococcus** (also known as *Streptococcus pyogenes*) is studded with **M protein**, a virulence factor that **inhibits phagocytosis**, prevents complement binding, and aids in epithelial attachment.

M protein is an alpha-helical coiled-coil protein that shares epitopes and **structural homology** with other alpha-helical coiled-coil proteins such as **tropomyosin and myosin**. In some patients, the protective antibodies against M protein that develop in *S pyogenes* acute infection may cross-react with myosin epitopes in the heart and cause **rheumatic carditis**.

(Choice A) Efflux pumps are generally globular proteins with multiple domains. They reside in the bacterial cell membrane and excrete toxic substances from the interior of the cell. Bacteria can use efflux pumps to generate antibiotic resistance to drugs that operate in the interior of the cell, such as fluoroquinolones and aminoglycosides.

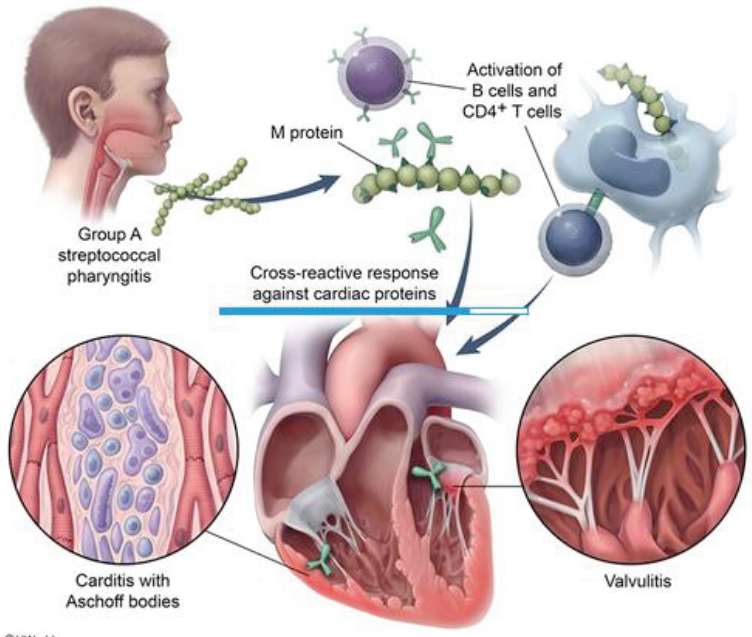
(Choices B and C) The bacterial cell wall of *S pyogenes* provides mechanical support and protects it from osmotic lysis. It is composed primarily of peptidoglycan, which forms a mesh-like, cross-linked polymer of

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Pathophysiology of acute rheumatic fever

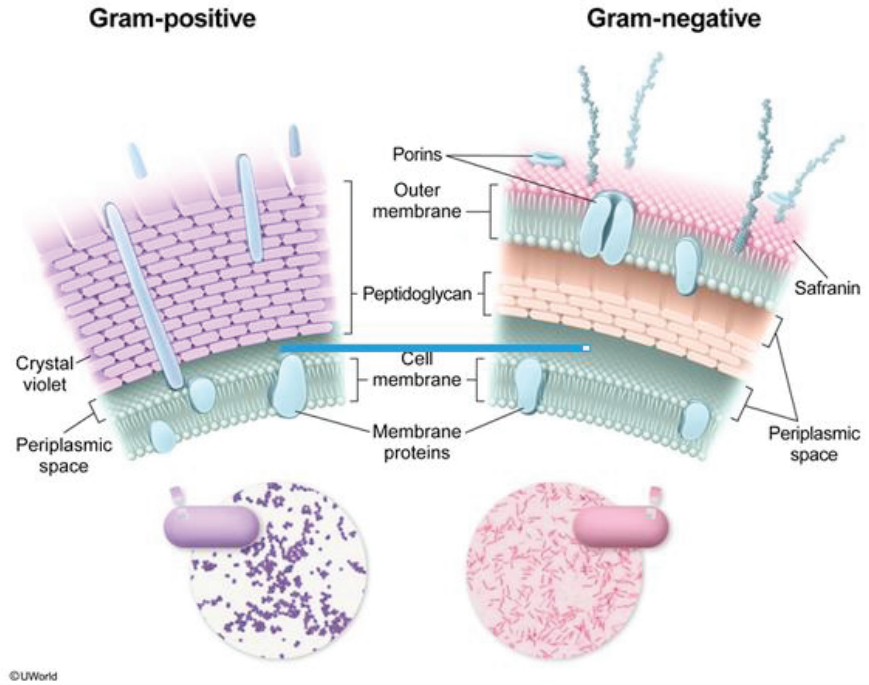


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pumps to generate antibiotic resistance to drugs that operate in the interior of the cell, such as fluoroquinolones and aminoglycosides.

(Choices B and C) The bacterial cell wall of *S pyogenes* provides mechanical support and protects it from osmotic lysis. It is composed primarily of peptidoglycan, which forms a mesh-like, cross-linked polymer of peptides and sugars.

(Choice E) Porins in the cell membrane aid in the movement of nutrients into bacterial cells. They are composed of protein strands that group together to form a barrel (beta-barrel).

Educational objective:

The major virulence factor of *Streptococcus pyogenes* is M protein, an alpha-helical coiled-coil protein that shares structural homology with tropomyosin and myosin. It extends from the cell wall and prevents phagocytosis, inhibits complement binding, and mediates bacterial adherence. Antibodies against M protein form shortly after acute infection and may cross-react with epitopes on myosin, leading to rheumatic carditis.

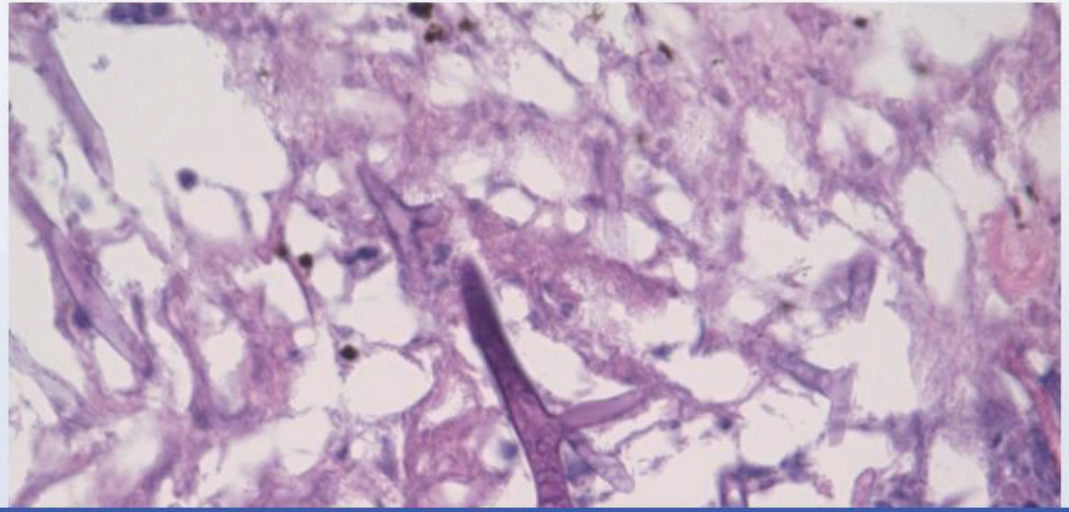
References

- M protein and other surface proteins on streptococci.

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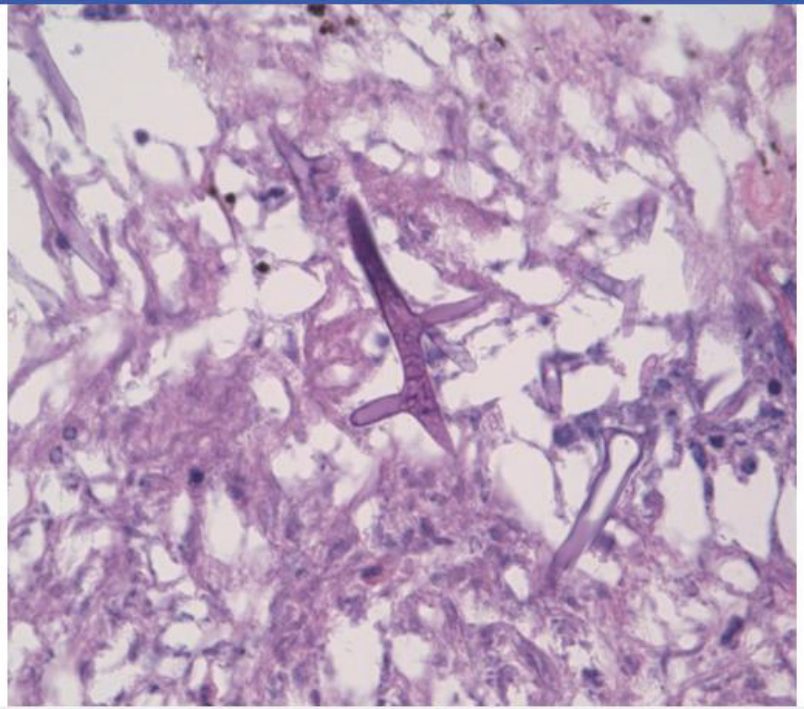
A 38-year-old man is undergoing treatment for acute myeloid leukemia. Initially, he had fevers and reported being lethargic and fatigued all the time. However, of late, he has noted increasingly severe right-sided headaches. He describes the pain to be throbbing in nature and located behind his right eye. He also has associated nasal stuffiness. The patient has no prior history of allergies. Physical examination reveals right-sided proptosis and periorbital tenderness. Biopsy of the right maxillary sinus mucosa reveals the following:



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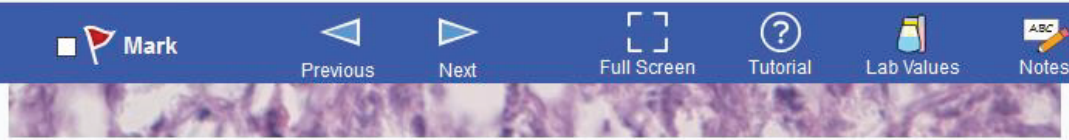
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Which of the following is the most likely cause of this patient's condition?

A. *Malassezia furfur*
B. *Microsporum canis*
C. *Rhizopus* species
D. *Aspergillus fumigatus*
E. *Candida albicans*
F. *Cryptococcus neoformans*
G. *Blastomyces dermatitidis*
H. *Histoplasma capsulatum*
I. *Coccidioides immitis*
J. *Sporothrix schenckii*

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Which of the following is the most likely cause of this patient's condition?

- A. *Malassezia furfur* (2%)
- B. *Microsporum canis* (0%)
- ✓ C. *Rhizopus* species (83%)
- D. *Aspergillus fumigatus* (7%)
- E. *Candida albicans* (1%)
- F. *Cryptococcus neoformans* (1%)
- G. *Blastomyces dermatitidis* (0%)
- H. *Histoplasma capsulatum* (0%)
- I. *Coccidioides immitis* (0%)
- J. *Sporothrix schenckii* (1%)

Correct

83%

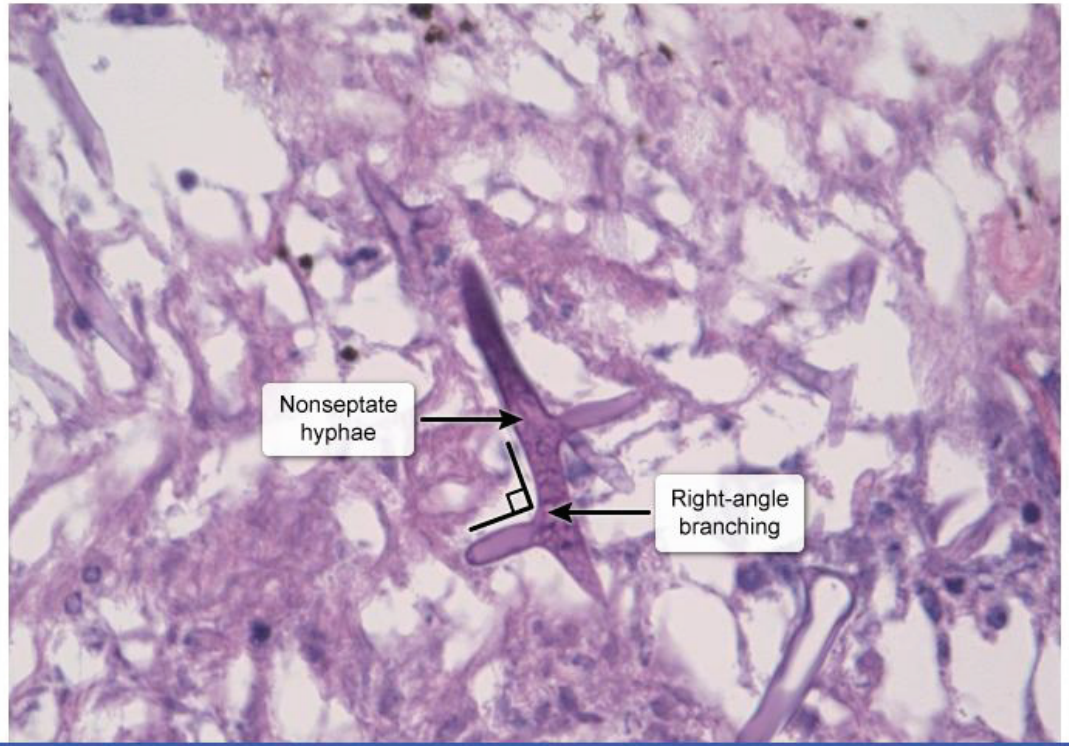
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Mucormycosis



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Mucor, *Rhizopus*, and *Absidia* species are saprophytic fungi present in the environment. They are transmitted by spore inhalation and cause **mucormycosis**. Mucormycosis is very strongly associated with **diabetic ketoacidosis**. Patients with underlying **immunosuppression** (eg, due to solid organ transplantation, hematologic malignancies, or glucocorticoid therapy) are also at high risk.

Mucormycosis tends to affect the **paranasal sinuses**. Symptoms include facial and periorbital pain, headache, and purulent nasal discharge. The fungi proliferate in the walls of blood vessels and cause necrosis of the corresponding tissue. Black eschar (necrotic tissue) may be seen on the palate or nasal turbinates.

Mucormycosis is diagnosed by light microscopy of a tissue specimen. *Mucor*, *Rhizopus*, and *Absidia* fungi exist in mold form only. They form broad, **nonseptate hyphae** that branch at **wide, often 90° angles**. Mucormycosis is treated by surgical debridement of necrotic tissue and amphotericin B.

(Choices A and B) *Malassezia furfur* and *Microsporum canis* cause cutaneous mycoses but do not affect the paranasal sinuses.

(Choice D) Invasive aspergillosis involving the paranasal sinuses can show close clinical resemblance to mucormycosis. However, light microscopy of the affected tissue will differentiate these two diagnoses:

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the paranasal sinuses.

(Choice D) Invasive aspergillosis involving the paranasal sinuses can show close clinical resemblance to mucormycosis. However, light microscopy of the affected tissue will differentiate these two diagnoses: unlike *Mucor* and *Rhizopus*, *Aspergillus* has septate hyphae that branch at 45° angles (V-shaped branching).

(Choice E) *Candida albicans* can cause a variety of symptoms in immunosuppressed patients. Right-sided endocarditis, renal abscesses, and esophagitis are among the most common. Budding yeasts and pseudohyphae are seen on light microscopy.

(Choice F) *Cryptococcus neoformans* primarily causes meningoencephalitis (eg, headache, confusion, altered mental state) in patients who are immunocompromised (particularly those with advanced AIDS).

(Choices G, H, and I) *Blastomyces, Histoplasma,* and *Coccidioides* cause lung disease in healthy patients. Disseminated disease occurs in immunosuppressed individuals. Isolated paranasal involvement is not typical.

(Choice J) *Sporothrix schenckii* can be transmitted to humans via subcutaneous inoculation. Manifestations include a papule at the site of exposure with subsequent papules forming along proximal lymphatic drainage pathways.

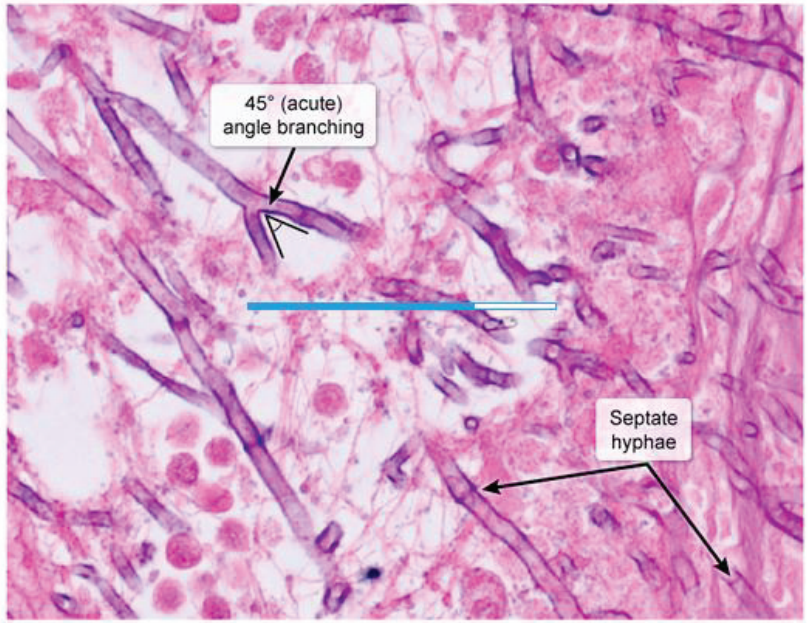
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the paranasal sinuses

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Aspergillus



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lymphatic drainage pathways.

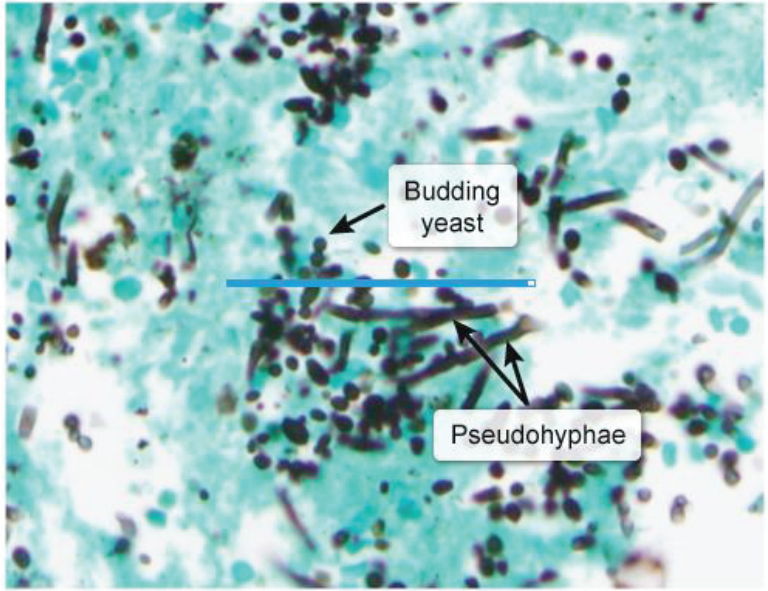
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the paranasal sinuses.

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Candida



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lymphatic drainage pathways.

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(Choice F) *Cryptococcus neoformans* primarily causes meningoencephalitis (eg, headache, confusion, altered mental state) in patients who are immunocompromised (particularly those with advanced AIDS).

(Choices G, H, and I) *Blastomyces, Histoplasma,* and *Coccidioides* cause lung disease in healthy patients. Disseminated disease occurs in immunosuppressed individuals. Isolated paranasal involvement is not typical.

(Choice J) *Sporothrix schenckii* can be transmitted to humans via subcutaneous inoculation. Manifestations include a papule at the site of exposure with subsequent papules forming along proximal lymphatic drainage pathways.

Educational objective:
Mucormycosis is an opportunistic infection caused by *Rhizopus*, *Mucor,* and *Absidia* species. The classic clinical picture is paranasal sinus involvement in a diabetic or immunosuppressed patient. The fungi form broad nonseptate hyphae that branch at right angles.

Microbiology	Infectious Diseases	Mucormycosis
Subject	System	Topic

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A 43-year-old man comes to the office due to fatigue and worsening pedal edema over the past several weeks. The patient was diagnosed with advanced HIV infection and started on antiretroviral therapy 3 months ago. He also has a history of hypertension. Physical examination shows bilateral lower extremity pitting edema. Serum creatinine is elevated and serum phosphorus is decreased compared to test results 3 months ago. Urinalysis reveals moderate proteinuria and glucosuria. Renal biopsy shows cytoplasmic vacuolization in the proximal tubules accompanied by loss of brush border and basement membrane denudation. Intracytoplasmic eosinophilic inclusions are also seen in the proximal tubules. There are no significant interstitial inflammatory infiltrates, and the glomeruli appear normal. Which of the following is the most likely diagnosis in this patient?

A. HIV-associated nephropathy
B. Hypertensive nephrosclerosis
C. Postinfectious glomerulonephritis
D. Tenofovir-induced nephrotoxicity
E. Trimethoprim-sulfamethoxazole–induced nephrotoxicity

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months ago. He also has a history of hypertension. Physical examination shows bilateral lower extremity pitting edema. Serum creatinine is elevated and serum phosphorus is decreased compared to test results 3 months ago. Urinalysis reveals moderate proteinuria and glucosuria. Renal biopsy shows cytoplasmic vacuolization in the proximal tubules accompanied by loss of brush border and basement membrane denudation. Intracytoplasmic eosinophilic inclusions are also seen in the proximal tubules. There are no significant interstitial inflammatory infiltrates, and the glomeruli appear normal. Which of the following is the most likely diagnosis in this patient?

A. HIV-associated nephropathy (18%)

B. Hypertensive nephrosclerosis (4%)

C. Postinfectious glomerulonephritis (3%)

D. Tenofovir-induced nephrotoxicity (55%)

E. Trimethoprim-sulfamethoxazole–induced nephrotoxicity (17%)

Correct

55%

55 secs

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This patient with HIV was recently started on antiretroviral therapy and subsequently developed evidence of proximal tubule dysfunction (eg, hypophosphatemia, glucosuria, proteinuria, biopsy abnormalities), raising concern for **tenofovir-induced nephrotoxicity**. Tenofovir is a common part of first-line HIV therapy. It is an adenosine analogue that is a member of the **nucleotide reverse transcriptase inhibitors** (NRTIs). NRTIs prevent reverse transcriptase from converting the HIV RNA genome into complementary double-stranded DNA, which inhibits viral replication.

Tenofovir is primarily eliminated via the proximal tubule cells of the kidney. High concentrations of tenofovir in these cells can interfere with mitochondrial DNA synthesis and result in cellular damage. This typically manifests with **acute kidney injury** (eg, elevated creatinine, water retention) and/or signs of **proximal tubule dysfunction** (eg, phosphaturia, glucosuria, proteinuria). Histopathology may show damage to proximal tubule cells (eg, loss of brush border, basement membrane denudation) and evidence of giant mitochondria (eg, large eosinophilic inclusions). Renal abnormalities typically improve once tenofovir is discontinued.

(Choice A) HIV-associated nephropathy is due to viral infection of kidney epithelial cells and typically manifests with hematuria, hypertension, and edema. Biopsy classically shows focal segmental glomerulosclerosis and significant interstitial inflammation.

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glomerulosclerosis and significant interstitial inflammation.

(Choice B) Hypertensive nephrosclerosis is most common in black patients who have markedly elevated blood pressure. It usually is characterized by proteinuria with or without renal insufficiency. Biopsy typically reveals damage to the renal vasculature (eg, intimal thickening, luminal narrowing), glomeruli (eg, glomerulosclerosis), and renal interstitium (eg, fibrosis, atrophy).

(Choice C) Poststreptococcal glomerulonephritis is an immune complex disease of the glomeruli caused by a preceding infection with a nephritogenic strain of group A beta-hemolytic streptococcus. Patients may have proteinuria, edema, hypertension, and/or acute kidney injury. However, they usually also have red/brown urine and biopsy evidence of diffuse proliferative glomerulonephritis.

(Choice E) Trimethoprim-sulfamethoxazole is often used in patients with advanced AIDS to prevent *Pneumocystis* pneumonia and/or *Toxoplasma gondii*. It can cause interstitial nephritis and acute kidney injury but does not usually cause focal damage to the proximal tubule.

Educational objective:
Tenofovir is a nucleotide reverse transcriptase inhibitor that is a common component of HIV therapy. This drug is generally well tolerated but may occasionally cause damage to the proximal tubule of the kidney, leading to acute kidney injury and/or proximal tubule impairment (eg, phosphoruria, glucosuria, proteinuria,

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glomerulosclerosis), and renal interstitium (eg, fibrosis, atrophy).

(Choice C) Poststreptococcal glomerulonephritis is an immune complex disease of the glomeruli caused by a preceding infection with a nephritogenic strain of group A beta-hemolytic streptococcus. Patients may have proteinuria, edema, hypertension, and/or acute kidney injury. However, they usually also have red/brown urine and biopsy evidence of diffuse proliferative glomerulonephritis.

(Choice E) Trimethoprim-sulfamethoxazole is often used in patients with advanced AIDS to prevent *Pneumocystis* pneumonia and/or *Toxoplasma gondii*. It can cause interstitial nephritis and acute kidney injury but does not usually cause focal damage to the proximal tubule.

Educational objective:
Tenofovir is a nucleotide reverse transcriptase inhibitor that is a common component of HIV therapy. This drug is generally well tolerated but may occasionally cause damage to the proximal tubule of the kidney, leading to acute kidney injury and/or proximal tubule impairment (eg, phosphoruria, glucosuria, proteinuria, water retention). Biopsy typically reveals a normal glomerulus and renal interstitium but damage to the proximal tubule.

Microbiology	Infectious Diseases	HIV
Subject	System	Topic

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A 56-year-old man with advanced AIDS comes to the emergency department due to several weeks of progressive fever, night sweats, weight loss, diarrhea, and generalized weakness. Physical examination shows mucosal pallor, generalized lymphadenopathy, and hepatosplenomegaly. Laboratory studies reveal anemia and elevated alkaline phosphatase and lactate dehydrogenase levels. CD4 count is 16/mm^3. Bone marrow biopsy shows aggregates of epithelioid histiocytes with foamy cytoplasm and numerous acid-fast intracellular organisms. Nucleic acid amplification test of the sample for *Mycobacterium tuberculosis* is negative. Which of the following pathogens is the most likely cause of this patient's illness?

A. *Cryptococcus neoformans*
B. *Cryptosporidium parvum*
C. *Legionella pneumophila*
D. *Mycobacterium avium*
E. *Mycobacterium marinum*
F. *Nocardia asteroides*

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progressive fever, night sweats, weight loss, diarrhea, and generalized weakness. Physical examination shows mucosal pallor, generalized lymphadenopathy, and hepatosplenomegaly. Laboratory studies reveal anemia and elevated alkaline phosphatase and lactate dehydrogenase levels. CD4 count is 16/mm^3. Bone marrow biopsy shows aggregates of epithelioid histiocytes with foamy cytoplasm and numerous acid-fast intracellular organisms. Nucleic acid amplification test of the sample for *Mycobacterium tuberculosis* is negative. Which of the following pathogens is the most likely cause of this patient's illness?

- A. ~~*Cryptococcus neoformans*~~ (4%)
- B. ~~*Cryptosporidium parvum*~~ (14%)
- C. ~~*Legionella pneumophila*~~ (1%)
- ✓ D. *Mycobacterium avium* (62%)
- E. *Mycobacterium marinum* (1%)
- F. *Nocardia asteroides* (14%)

Correct

62%

01 min, 32 secs

10/05/2020

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This patient's subacute systemic symptoms (eg, fever, night sweats, weight loss, weakness), lymphadenopathy, hepatosplenomegaly, elevated alkaline phosphatase, and intracellular acid-fast bacteria raise strong suspicion for disseminated ***Mycobacterium avium* complex (MAC)**. MAC is an infection caused by the **nontuberculous** mycobacteria *M avium* and *Mycobacterium intracellulare*. Although these infections can occur in both immunocompetent and immunosuppressed hosts, most cases arise in patients with untreated AIDS who have **CD4 counts <50/mm^3**.

MAC organisms are acquired by ingestion or inhalation. They are phagocytosed by macrophages but initially evade destruction due to microbial virulence factors that prevent phagolysosome formation. In healthy individuals, the infection is controlled with the cell-mediated immune response. However, in patients with **advanced AIDS**, the body is unable to generate sufficient CD4-mediated cytokines (eg, interferon-gamma) to activate macrophages, which allows the pathogen to spread through the bloodstream and reticuloendothelial system.

Most patients with disseminated infection have nonspecific symptoms (eg, fever, weight loss, diarrhea). Widespread involvement of the **reticuloendothelial system** often causes anemia, hepatosplenomegaly, and/or elevated alkaline phosphatase and lactate dehydrogenase. The diagnosis is usually made with blood cultures, but results may take weeks because mycobacteria grow slowly. Histologic findings in the

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Widespread involvement of the **reticuloendothelial system** often causes anemia, hepatosplenomegaly, and/or elevated alkaline phosphatase and lactate dehydrogenase. The diagnosis is usually made with blood cultures, but results may take weeks because mycobacteria grow slowly. Histologic findings in the bone marrow include foamy macrophages with **intracellular, acid-fast bacilli**. Granulomata may be seen.

(Choice A) *Cryptococcus neoformans*, an encapsulated yeast, is a common cause of meningoencephalitis in patients with advanced AIDS. Although it is a facultative intracellular pathogen, it does not stain with acid-fast preparations. The pathogen is usually visualized with India ink, mucicarmine, or methenamine stains.

(Choice B) *Cryptosporidium parvum* is a common cause of high-volume diarrhea and biliary disease in patients with advanced AIDS. This organism's oocytes can be visualized with modified acid-fast stain, and the pathogen is intracellular. However, it infects epithelial cells and does not spread through the reticuloendothelial system to the bone marrow or lymph nodes.

(Choice C) *Legionella pneumophila* is a gram-negative, intracellular bacteria that often causes gastrointestinal symptoms prior to pneumonia. However, it does not stain with acid-fast and does not generally cause lymphadenopathy or bone marrow infection.

(Choice E) *Mycobacterium marinum* is a nontuberculous mycobacterium that can cause skin and soft

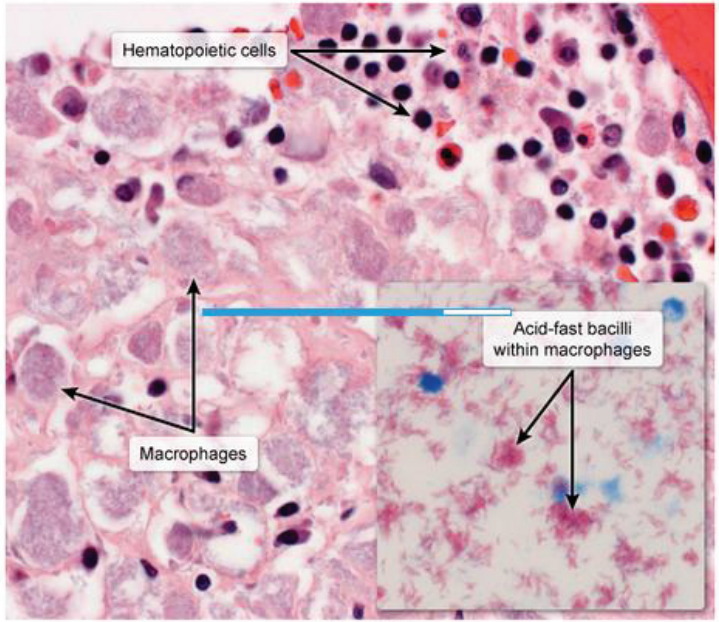
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Widespread involvement of the **reticuloendothelial system** often causes anemia, hepatosplenomegaly,

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***Mycobacterium avium* complex (MAC)**



Bone marrow

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generally cause lymphadenopathy or bone marrow infection.

(Choice E) *Mycobacterium marinum* is a nontuberculous mycobacterium that can cause skin and soft tissue infection following exposure to water (eg, fish tanks). It does not generally cause several weeks of diarrhea, lymphadenopathy, and hepatosplenomegaly.

(Choice F) *Nocardia asteroides*, a partially acid-fast organism, typically causes pneumonia and/or brain abscess. Gastrointestinal symptoms, lymphadenopathy, and bone marrow involvement would be atypical.

Educational objective:

Mycobacterium avium complex (MAC) infections are common in patients with advanced AIDS. The bacterium often spreads through the bloodstream and reticuloendothelial system and causes nonspecific symptoms (eg, fever, fatigue, weight loss, diarrhea), lymphadenopathy, and hepatosplenomegaly. Diagnosis is often made on blood culture or bone marrow aspirate (intracellular acid-fast bacteria that are not *Mycobacterium tuberculosis*).

Pharmacology	Infectious Diseases	Nontuberculous mycobacterial diseases
Subject	System	Topic

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A 27-year-old man comes to the office due to a 2-week history of genital papules that are not painful or pruritic. Over this period, he has also had fatigue and mild, generalized arthralgia but no urethral discharge or dysuria. The patient had gonococcal urethritis 3 months ago, which was adequately treated, and tests for other sexually transmitted infections at that time were negative. He is sexually active with several male and female partners and reports using condoms consistently after the episode of gonorrhea. Temperature is 37.6 C (99.6 F). Physical examination shows a faint, diffuse maculopapular skin rash involving the trunk, extremities, palms, and soles. There are several enlarged, nontender inguinal lymph nodes. Genital examination reveals multiple elevated lesions on the scrotum and perineal region. Histopathologic evaluation of these lesions would most likely reveal which of the following in this patient?

A. Acantholysis with superficial dermal lymphocytic infiltrate
B. Dysplastic spindle cells with viral genome that form vascular channels
C. Intense plasma cell–rich infiltrate with proliferative endarteritis
D. Panniculitis and septal inflammation with multinucleated giant cells
E. Papillomatous epidermal hyperplasia with cytoplasmic vacuolization

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or dysuria. The patient had gonococcal urethritis 3 months ago, which was adequately treated, and tests for other sexually transmitted infections at that time were negative. He is sexually active with several male and female partners and reports using condoms consistently after the episode of gonorrhea. Temperature is 37.6 C (99.6 F). Physical examination shows a faint, diffuse maculopapular skin rash involving the trunk, extremities, palms, and soles. There are several enlarged, nontender inguinal lymph nodes. Genital examination reveals multiple elevated lesions on the scrotum and perineal region. Histopathologic evaluation of these lesions would most likely reveal which of the following in this patient?

- A. Acantholysis with superficial dermal lymphocytic infiltrate (12%)
- B. ~~Dysplastic spindle cells with viral genome that form vascular channels~~ (5%)
- C. Intense plasma cell–rich infiltrate with proliferative endarteritis (44%)
- D. ~~Panniculitis and septal inflammation with multinucleated giant cells~~ (11%)
- E. Papillomatous epidermal hyperplasia with cytoplasmic vacuolization (24%)

Incorrect
Correct answer

44%

02 mins, 46 secs

12/15/2020

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Syphilis manifestations	
Primary	• Painless genital ulcer (chancre)
Secondary	• Diffuse rash (palms & soles) • Lymphadenopathy (epitrochlear) • Condyloma latum • Oral lesions • Hepatitis
Latent	• Asymptomatic
Tertiary	• CNS (tabes dorsalis, dementia) • Cardiovascular (aortic aneurysm/insufficiency) • Cutaneous (gummas)

CNS = central nervous system.

Secondary syphilis is characterized by the spread of the causative spirochete, *Treponema pallidum*, through the blood to the skin and mucosal surfaces. Patients usually have a diffuse **maculopapular skin**

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Secondary syphilis is characterized by the spread of the causative spirochete, *Treponema pallidum*, through the blood to the skin and mucosal surfaces. Patients usually have a diffuse **maculopapular skin rash** that includes the palms and soles. They may also develop **condylomata lata**, which are painless, wart-like, elevated plaques, on moist areas of the skin such as the scrotum and perineum. **Lymphadenopathy**, fatigue, arthralgias, and mild fever are also common. Histopathologic examination of syphilitic lesions (at all stages) classically demonstrates **proliferative endarteritis** of small vessels with a surrounding plasma cell–rich infiltrate.

This patient was likely infected with syphilis at the same time he was infected with gonorrhea (coinfection is common). Serologic testing for syphilis (eg, rapid plasma reagin) is often falsely negative in early infection due to lag time between acquisition of *T pallidum* and the development of a measurable humoral antibody response. Patients who do not notice or ignore the genital chancre of primary syphilis often develop secondary syphilis 2 – 10 weeks later.

(Choice A) Pemphigus vulgaris is characterized by autoantibodies against epithelial cell surface antigens, leading to the formation of mucous membrane blisters that quickly erode; histopathology usually shows acantholysis (detached keratinocytes) with superficial dermal infiltrate.

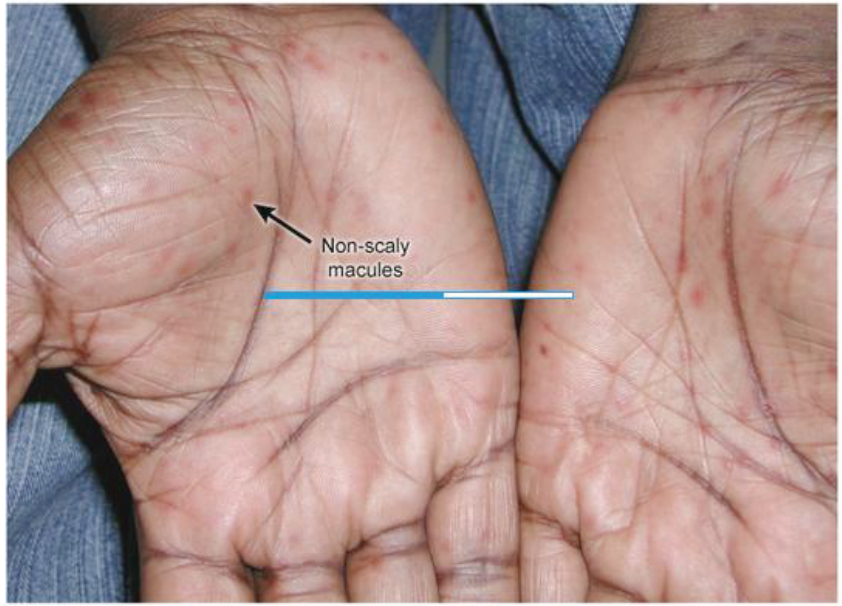
(Choice B) Kaposi sarcoma (KS) lesions are histologically characterized by spindle-shaped endothelial

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Secondary syphilis



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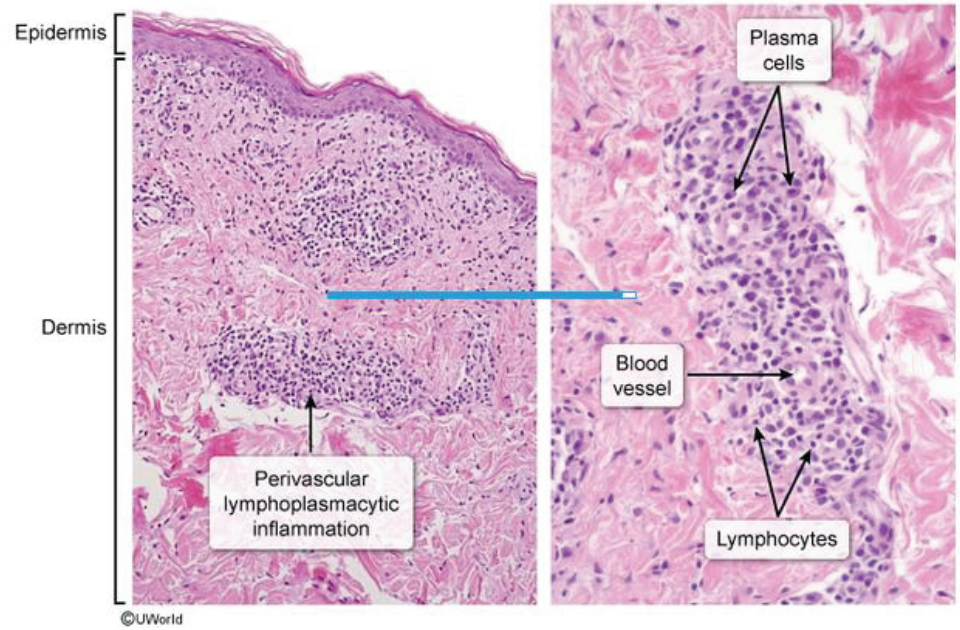
(Choice B) Kaposi sarcoma (KS) lesions are histologically characterized by spindle-shaped endothelial

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Syphilis



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(Choice B) Kaposi sarcoma (KS) lesions are histologically characterized by spindle-shaped endothelial

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(Choice B) Kaposi sarcoma (KS) lesions are histologically characterized by spindle-shaped endothelial cells that form vascular channels. KS is due to human herpesvirus 8 infection and most commonly occurs in the setting of advanced AIDS. Lesions typically appear as purplish or dark brown plaques and nodules on the lower extremities.

(Choice D) Biopsy of erythema nodosum lesions usually reveals septal panniculitis with multinucleated giant cells. Erythema nodosum is a delayed-type hypersensitivity reaction that can occur due to drugs or other antigenic stimuli. Patients usually present with tender nodules on the bilateral shins.

(Choice E) Biopsy of anogenital warts will demonstrate papillomatous epidermal hyperplasia with cytoplasmic vacuolization. Anogenital warts are caused by specific serotypes of human papillomavirus (eg, HPV-6, HPV-11). Anogenital warts are not typically associated with diffuse maculopapular rash or systemic symptoms.

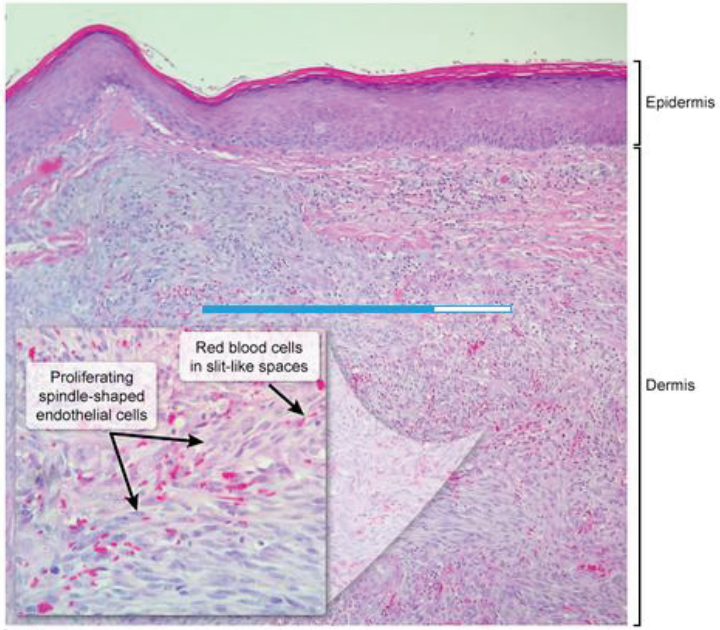
Educational objective:
Histopathologic examination of syphilitic lesions classically demonstrates a proliferative endarteritis with a surrounding plasma cell infiltrate. Most of the manifestations of syphilis are due to localized tissue ischemia resulting from endarteritis.

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Kaposi sarcoma



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Kaposi sarcoma



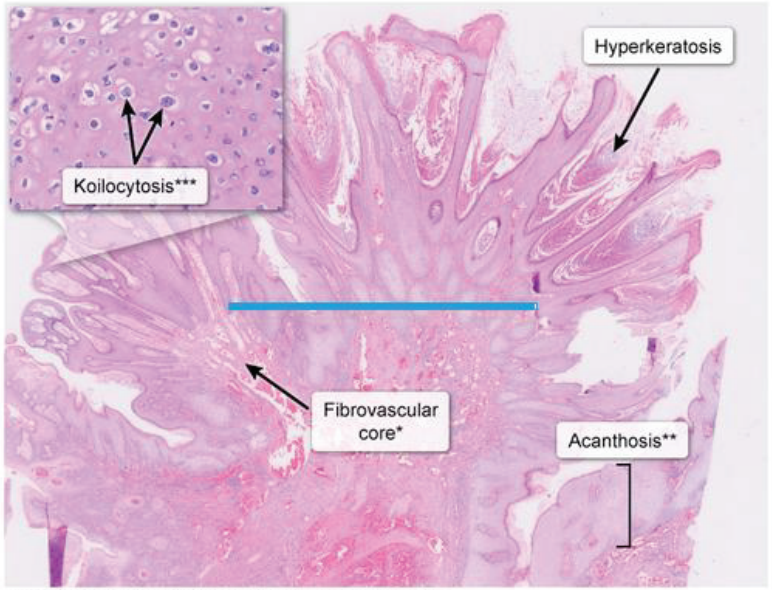
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Condyloma acuminatum



*Papillary architecture shows fibrovascular cores lined by epithelial cells
**Thickened epidermis
***Irregular nuclei with perinuclear halos

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A 19-year-old woman comes to the office due to 2 days of dysuria, urinary frequency, and urgency. The symptoms began a day after having sexual intercourse with her boyfriend. The patient has no fever, flank pain, nausea, or vomiting. She has no chronic medical conditions and no known drug allergies. Vital signs are within normal limits. Examination shows mild suprapubic tenderness. Urinalysis reveals many bacteria and white blood cells/hpf. Which of the following is the most appropriate pharmacotherapy for this patient?

- A. Azithromycin
- B. Doxycycline
- C. Fluconazole
- D. Metronidazole
- E. Trimethoprim-sulfamethoxazole

Submit

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A 19-year-old woman comes to the office due to 2 days of dysuria, urinary frequency, and urgency. The symptoms began a day after having sexual intercourse with her boyfriend. The patient has no fever, flank pain, nausea, or vomiting. She has no chronic medical conditions and no known drug allergies. Vital signs are within normal limits. Examination shows mild suprapubic tenderness. Urinalysis reveals many bacteria and white blood cells/hpf. Which of the following is the most appropriate pharmacotherapy for this patient?

- ✗ A. Azithromycin (12%)
- B. Doxycycline (6%)
- C. Fluconazole (0%)
- D. Metronidazole (6%)
- ✓ E. Trimethoprim-sulfamethoxazole (74%)

Incorrect
Correct answer
E

74%
Answered correctly

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Time Spent

01/31/2021
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This patient's acute dysuria, urinary frequency/urgency, suprapubic tenderness, and pyuria/bacteriuria indicate **acute simple cystitis**. Women are at greater risk than men due to the short distance between the anus and vaginal introitus, which allows enteric bacteria to contaminate the urethra and ascend into the bladder. **Recent sexual intercourse** is the single greatest risk factor in otherwise healthy women.

Most cases of acute simple cystitis are caused by the enteric bacteria ***Escherichia coli***. However, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Staphylococcus saprophyticus* are also frequently isolated. Patients with no risk factors for resistant bacteria (eg, recent inpatient hospitalization or antibiotic use) are generally treated empirically with 3-6 days of nitrofurantoin or **trimethoprim-sulfamethoxazole** (TMP-SMX) due to their excellent efficacy and low risk of side effects.

(Choices A and B) Azithromycin and doxycycline treat *Chlamydia trachomatous* infections of the urogenital tract. Most cases of chlamydia are asymptomatic, but some patients have dysuria and urinary frequency. Although urinalysis will reveal pyuria, no bacteria would be seen on urinary Gram stain because *C trachomatous* has no cell wall. Neither azithromycin nor doxycycline adequately treats enteric, gram-negative pathogens; therefore, neither is typically used for acute simple cystitis.

(Choice C) Fluconazole is often used to treat vaginal candidiasis, which can cause dysuria and is often

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negative pathogens; therefore, neither is typically used for acute simple cystitis.

(Choice C) Fluconazole is often used to treat vaginal candidiasis, which can cause dysuria and is often linked to vaginal intercourse. However, most patients also have vaginal itching and soreness. The presence of urinary frequency, urgency, and pyuria/bacteriuria makes bacterial cystitis more likely.

(Choice D) Metronidazole can treat *Trichomonas vaginalis*, a flagellated protozoan that is transmitted during sexual intercourse. Women infected with trichomonas often have dysuria and frequency, but most also have a purulent, malodourous vaginal discharge. The presence of pyuria/bacteriuria on urinalysis makes acute bacterial cystitis more likely.

Educational objective:
Acute simple cystitis often occurs in young, otherwise healthy women, particularly following sexual intercourse. Common manifestations include dysuria, urinary frequency/urgency, and urinalysis evidence of pyuria/bacteriuria. Empiric treatment with nitrofurantoin or trimethoprim-sulfamethoxazole is typically curative.

Pharmacology	Infectious Diseases	Urinary tract infection
Subject	System	Topic

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A 43-year-old man comes to the office after a recent hospitalization for *Pneumocystis* pneumonia. The patient is taking trimethoprim-sulfamethoxazole and says that his pulmonary symptoms are better. He has a history of HIV and was on highly active antiretroviral therapy until self-discontinuing treatment 2 years ago. On physical examination, the patient appears to be in no acute distress. BMI is 20 kg/m^2. A few crackles are heard at the lung bases. His most recent CD4 count is 122/mm^3. After discussing medical compliance and the need to resume antiretroviral therapy, HIV genotyping assay is performed. Additional testing for HLA-B*57:01 yields positive results. Which of the following medications is contraindicated in this patient due to the risk of a potentially fatal hypersensitivity reaction?

A. Abacavir
B. Darunavir
C. Efavirenz
D. Emtricitabine
E. Nevirapine

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patient is taking trimethoprim-sulfamethoxazole and says that his pulmonary symptoms are better. He has a history of HIV and was on highly active antiretroviral therapy until self-discontinuing treatment 2 years ago. On physical examination, the patient appears to be in no acute distress. BMI is 20 kg/m^2. A few crackles are heard at the lung bases. His most recent CD4 count is 122/mm^3. After discussing medical compliance and the need to resume antiretroviral therapy, HIV genotyping assay is performed. Additional testing for HLA-B*57:01 yields positive results. Which of the following medications is contraindicated in this patient due to the risk of a potentially fatal hypersensitivity reaction?

- ✓ A. Abacavir (52%)
- B. Darunavir (6%)
- C. Efavirenz (18%)
- D. Emtricitabine (12%)
- E. Nevirapine (9%)

Correct

52%
Answered correctly

20 secs
Time Spent

12/27/2020
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Abacavir is a nucleoside reverse transcriptase inhibitor (NRTI) used in the treatment of HIV/AIDS. Allergic responses can occur with many HIV/AIDS medications. **Abacavir hypersensitivity reaction** (AHR) is an allergic reaction that develops in 2%–8% of patients and is strongly associated with the HLA-B*57:01 allele of the human leukocyte antigen (HLA) system. AHR occurs due to direct binding of abacavir to a segment on the **HLA-B*57:01** molecule, which alters the presentation of self-peptides to the immune system and results in a **delayed hypersensitivity reaction** (type IV). Manifestations are mediated by a cytotoxic T-cell response and typically include fever, malaise, gastrointestinal symptoms, and a delayed rash. Abacavir discontinuation results in rapid improvement. A negative test for the HLA-B*57:01 allele has almost a 100% negative predictive value for AHR. Therefore, genetic testing is usually done prior to administering the medication.

(Choice B) Common side effects of protease inhibitors such as darunavir include metabolic abnormalities (hyperglycemia), gastrointestinal symptoms, and lipodystrophy.

(Choices C and E) The non-NRTIs efavirenz and nevirapine may cause Stevens-Johnson syndrome and toxic epidermal necrolysis, but these conditions are not associated with HLA alleles. Liver function abnormalities can also occur with these 2 non-NRTIs.

(Choice D) Emtricitabine, another NRTI, has been associated with an asymptomatic macular rash on the

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(Choice D) Emtricitabine, another NRTI, has been associated with an asymptomatic macular rash on the

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(Choices C and E) The non-NRTIs efavirenz and nevirapine may cause Stevens-Johnson syndrome and toxic epidermal necrolysis, but these conditions are not associated with HLA alleles. Liver function abnormalities can also occur with these 2 non-NRTIs.

(Choice D) Emtricitabine, another NRTI, has been associated with an asymptomatic macular rash on the palms or soles; no genetic basis for this reaction has been identified.

Educational objective:

Abacavir hypersensitivity reaction occurs in 2%–8% of patients and is strongly associated with the HLA-B*57:01 allele.

References

- Abacavir pharmacogenetics—from initial reports to standard of care.
- Hypersensitivity reactions to HIV therapy.

Pharmacology	Infectious Diseases	Antiretroviral therapy
Subject	System	Topic

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A 19-year-old man comes to the office with an ulcer on his penis. The patient first noticed the lesion 3 days ago. His temperature is 37.1 C (98.8 F). Physical examination shows an indurated and painless ulcer near the glans penis, with no surrounding erythema and no inguinal lymphadenopathy. The patient is a college student. He has no significant past medical history and takes no medications. He has no known drug allergies. The first-line treatment for this patient has structural similarities with which of the following?

A. D-alanine-D-alanine
B. D-glutamic acid-D-glutamic acid
C. Folic acid
D. L-alanine-D-glutamine
E. N-acetylglucosamine
F. N-acetylmuramic acid

Submit

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A 19-year-old man comes to the office with an ulcer on his penis. The patient first noticed the lesion 3 days ago. His temperature is 37.1 C (98.8 F). Physical examination shows an indurated and painless ulcer near the glans penis, with no surrounding erythema and no inguinal lymphadenopathy. The patient is a college student. He has no significant past medical history and takes no medications. He has no known drug allergies. The first-line treatment for this patient has structural similarities with which of the following?

- A. D-alanine-D-alanine (62%)
- B. D-glutamic acid-D-glutamic acid (5%)
- C. Folic acid (3%)
- D. L-alanine-D-glutamine (6%)
- E. N-acetylglucosamine (10%)
- F. N-acetylmuramic acid (11%)

Correct

62% Answered correctly

01 min, 06 secs Time Spent

10/05/2020 Last Updated

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This patient likely has a chancre due to **primary syphilis**, a sexually transmitted infection caused by the spirochete *Treponema pallidum*. Spirochetes are universally sensitive to **penicillin** because they are all gram-negative organisms with a peptidoglycan cell wall.

Penicillins work by covalently binding to and inhibiting **transpeptidase**. This enzyme catalyzes the final **cross-linking** step in peptidoglycan cell wall formation: the joining of the amino acid in the third position of a peptidoglycan molecule to the terminal D-alanine-D-alanine of another peptidoglycan molecule. The structural similarity of penicillins to D-alanine-D-alanine likely facilitates their binding to transpeptidase. When transpeptidase is inhibited, cell wall synthesis ceases and cell wall degradation by bacterial autolysins proceeds unchecked. The weakened cell wall integrity causes osmotic lysis of the bacterium.

Vancomycin, a glycopeptide antibiotic, **directly** binds to the D-alanine-D-alanine residues, preventing the incorporation of new subunits into the cell wall. Vancomycin acts at an earlier stage of cell wall formation than do the penicillins.

(Choices B and D) D-glutamic acid-D-glutamic acid and L-alanine-D-glutamine are not sequences targeted by transpeptidase. Penicillin is not a structural analog of either molecule.

(Choice C) Sulfonamide antibiotics are antimetabolites that compete with para-aminobenzoic acid for incorporation into folic acid. Trimethoprim blocks another step in folic acid synthesis by inhibiting the

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than do the penicillins.

(Choices B and D) D-glutamic acid-D-glutamic acid and L-alanine-D-glutamine are not sequences targeted by transpeptidase. Penicillin is not a structural analog of either molecule.

(Choice C) Sulfonamide antibiotics are antimetabolites that compete with para-aminobenzoic acid for incorporation into folic acid. Trimethoprim blocks another step in folic acid synthesis by inhibiting the enzyme dihydrofolate reductase.

(Choices E and F) Peptidoglycan precursor molecules consist of a disaccharide composed of N-acetylmuramic acid (MurNAc) and N-acetylglucosamine (GlcNAc).

Educational objective:
Penicillins, structurally similar to D-alanine-D-alanine, inhibit transpeptidase by binding covalently to its active site. The result is failed synthesis of the bacterial peptidoglycan cell wall.

Microbiology	Infectious Diseases	Syphilis
Subject	System	Topic

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A previously healthy 23-year-old man comes to the office due to abrupt-onset high fever, chills, headache, and weakness that developed during a hiking and camping trip in New Mexico. His initial symptoms were quickly followed by intensely painful swellings in the groin. Physical examination shows tender and enlarged inguinal lymph nodes with overlying erythematous skin. Blood cultures and fluid aspirated from the lymph nodes grow gram-negative coccobacilli, which resemble a closed safety pin on special staining. Which of the following are the most likely source of this patient's infection?

A. Bats
B. Poultry
C. Rodents
D. Sheep
E. Swine

Submit

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A previously healthy 23-year-old man comes to the office due to abrupt-onset high fever, chills, headache, and weakness that developed during a hiking and camping trip in New Mexico. His initial symptoms were quickly followed by intensely painful swellings in the groin. Physical examination shows tender and enlarged inguinal lymph nodes with overlying erythematous skin. Blood cultures and fluid aspirated from the lymph nodes grow gram-negative coccobacilli, which resemble a closed safety pin on special staining. Which of the following are the most likely source of this patient's infection?

- A. ~~Bats~~ (6%)
- B. ~~Poultry~~ (5%)
- ✓ C. Rodents (77%)
- D. Sheep (7%)
- E. Swine (3%)

Correct

77% Answered correctly

54 secs Time Spent

02/10/2021 Last Updated

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This patient's acute febrile illness with tender, erythematous inguinal lymphadenopathy likely indicates **bubonic plague**, a zoonotic infection endemic to the Southwestern United States (eg, New Mexico). The causative pathogen is ***Yersinia pestis***, a gram-negative coccobacillus that exhibits **bipolar staining** (resembling a safety pin) on Giemsa or Wright stain. Although many small mammals can harbor the bacteria, **rodents** (eg, rats) are the primary environmental reservoir. Transmission to humans primarily occurs via rodent **flea bite**.

Following cutaneous injection, the organism travels to regional lymph nodes and triggers a significant inflammatory reaction. Manifestations typically begin with acute fever, chills, weakness, and headache; **buboes** (painful, swollen, erythematous lymph nodes) develop shortly thereafter. Treatment with antibiotics (eg, aminoglycoside) is generally curative.

(Choice A) Bats can transmit rabies, which is characterized by nonspecific symptoms (eg, fever, myalgias, malaise) followed by hydrophobia, pharyngeal spasms, hyperactivity, coma, and death. Rabies is caused by a virus (*Lyssavirus*), not a gram-negative coccobacillus.

(Choice B) Non-typhoidal *Salmonella*, a motile gram-negative bacillus, is often transmitted via the ingestion of contaminated poultry. It causes febrile ("pea soup") diarrhea, not acute regional inflammatory lymphadenopathy.

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ingestion of contaminated poultry. It causes febrile ("pea soup") diarrhea, not acute regional inflammatory lymphadenopathy.

(Choice D) Sheep hides can transmit anthrax, which is typically characterized by a necrotic skin ulcer with extensive surrounding edema and regional lymphadenopathy. *Bacillus anthracis*, the causative agent, is a gram-positive, spore-forming rod; infections are quite rare in the United States.

(Choice E) *Trichinella*, a roundworm transmitted by ingesting contaminated swine, is often associated with transient gastrointestinal symptoms followed by skeletal muscle pain, tenderness, swelling, and weakness.

Educational objective:
Bubonic plague is a zoonotic infection that causes febrile illness with regional inflammatory lymphadenopathy (buboes). The underlying pathogen is *Yersinia pestis*, a gram-negative coccobacillus that exhibits bipolar staining (resembling a closed safety pin). The major environmental reservoir is rodents, and transmission usually occurs via rodent flea bite.

References

- Plague.

Microbiology Infectious Diseases Plague

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www.ncbi.nlm.nih.gov/pubmed/17416264

A 32-year-old man with HIV is diagnosed with pulmonary tuberculosis and started on a 4-drug combination therapy. On a follow-up visit 3 weeks later, he reports red urine and red staining of his contact lenses. A drug susceptibility test of his sputum isolates of *Mycobacterium tuberculosis* shows resistance to several antimycobacterial agents. Which of the following best explains the bacterial resistance to the drug responsible for this patient's current symptoms?

A. Altered structure of enzymes involved in bacterial DNA winding-unwinding
B. Altered structure of enzymes involved in bacterial RNA synthesis
C. Altered structure of bacterial ribosomal proteins
D. Decreased activity of bacterial catalase-peroxidase
E. Upregulation of bacterial beta-lactamase synthesis

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A 32-year-old man with HIV is diagnosed with pulmonary tuberculosis and started on a 4-drug combination therapy. On a follow-up visit 3 weeks later, he reports red urine and red staining of his contact lenses. A drug susceptibility test of his sputum isolates of *Mycobacterium tuberculosis* shows resistance to several antimycobacterial agents. Which of the following best explains the bacterial resistance to the drug responsible for this patient's current symptoms?

A. ~~Altered structure of enzymes involved in bacterial DNA winding-unwinding~~ (5%)

✓ B. Altered structure of enzymes involved in bacterial RNA synthesis (70%)

C. Altered structure of bacterial ribosomal proteins (15%)

D. ~~Decreased activity of bacterial catalase-peroxidase~~ (7%)

E. ~~Upregulation of bacterial beta-lactamase synthesis~~ (1%)

Correct

70%
Answered correctly

59 secs
Time Spent

01/24/2021
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Drugs for treatment of tuberculosis		
Drug	**Mechanism of action**	**Side effects**
(R)ifampin	Inhibition of bacterial DNA-dependent RNA polymerase	GI side effects, rash, red-orange body fluids, cytopenias
(I)soniazid	Inhibition of mycolic acid synthesis	Neurotoxicity (give vitamin B_6/pyridoxine), hepatotoxicity
(P)yrazinamide	Unclear	Hepatotoxicity, hyperuricemia
(E)thambutol	Inhibition of arabinosyl transferase (?)	Optic neuropathy

GI = gastrointestinal.

This patient with HIV has active **pulmonary tuberculosis**, typically treated with a 4-drug combination of a rifamycin (eg, rifampin, rifabutin), isoniazid, pyrazinamide, and ethambutol (RIPE therapy). The **rifamycins**

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This patient with HIV has active **pulmonary tuberculosis**, typically treated with a 4-drug combination of a rifamycin (eg, rifampin, rifabutin), isoniazid, pyrazinamide, and ethambutol (RIPE therapy). The **rifamycins** commonly cause **harmless red-orange discoloration** of body fluids (urine, sweat, saliva, tears), which explains this patient's symptoms. They inhibit DNA-dependent **RNA polymerase**, thereby preventing transcription and leading to a deficiency of proteins necessary for mycobacterial survival. Structural alteration of this DNA-dependent RNA polymerase induces bacterial **resistance**. Unlike isoniazid, rifamycins are not specific to mycobacteria.

(Choice A) Structural alteration of enzymes involved in DNA winding-unwinding would promote resistance to fluoroquinolones, drugs that bind and inhibit DNA gyrase in bacterial cells, causing fracture of the DNA chain.

(Choice C) Antibiotics that act on the ribosome can be divided into those that act on the 50S subunit (eg, chloramphenicol, clindamycin, linezolid, macrolides) and those that act on the smaller 30S subunit (tetracycline, doxycycline, aminoglycosides).

(Choice D) Decreased bacterial catalase-peroxidase activity is a mycobacterial response to isoniazid. Before it can inhibit mycolic acid synthesis, isoniazid must be converted to its active form by the mycobacterial catalase-peroxidase enzyme.

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chloramphenicol, clindamycin, linezolid, macrolides) and those that act on the smaller 30S subunit (tetracycline, doxycycline, aminoglycosides).

(Choice D) Decreased bacterial catalase-peroxidase activity is a mycobacterial response to isoniazid. Before it can inhibit mycolic acid synthesis, isoniazid must be converted to its active form by the mycobacterial catalase-peroxidase enzyme.

(Choice E) Upregulation of beta-lactamase synthesis would cause bacterial resistance to beta-lactam drugs such as penicillins, aminopenicillins, cephalosporins, and monobactams. Infections caused by organisms expressing beta-lactamase require the addition of a beta-lactamase inhibitor (eg, clavulanic acid, sulbactam, tazobactam) or the use of a carbapenem.

Educational objective:
The rifamycins block the action of the bacterial DNA-dependent RNA polymerase, thereby inhibiting transcription. Resistance is acquired by modification of the rifampin binding site on the bacterial DNA-dependent RNA polymerase. Common side effects include hepatotoxicity, blood dyscrasias, and harmless red-orange discoloration of body fluids.

Pharmacology	Infectious Diseases	Tuberculosis
Subject	System	Topic

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A 30-year-old man comes to the emergency department due to a week of fever, chills, and generalized malaise. The patient uses intravenous heroin and has been hospitalized several times due to skin and soft tissue infections. Cardiac auscultation shows a systolic ejection murmur, and subsequent echocardiography reveals a vegetative lesion of the aortic valve. Blood cultures from admission grow *Enterococcus faecalis*; subsequent testing reveals D-lactate rather than D-alanine as the terminal amino acid in the bacteria's pentapeptide peptidoglycan cell wall precursor. This substitution is likely to significantly decrease the efficacy of which of the following antibiotics?

A. Ceftriaxone
B. Fosfomycin
C. Penicillin
D. Polymyxin
E. Tetracycline
F. Vancomycin

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malaise. The patient uses intravenous heroin and has been hospitalized several times due to skin and soft tissue infections. Cardiac auscultation shows a systolic ejection murmur, and subsequent echocardiography reveals a vegetative lesion of the aortic valve. Blood cultures from admission grow *Enterococcus faecalis*; subsequent testing reveals D-lactate rather than D-alanine as the terminal amino acid in the bacteria's pentapeptide peptidoglycan cell wall precursor. This substitution is likely to significantly decrease the efficacy of which of the following antibiotics?

- A. ~~Ceftriaxone~~ (1%)
- B. ~~Fosfomycin~~ (0%)
- C. Penicillin (12%)
- D. Polymyxin (0%)
- E. Tetracycline (0%)
- ✓ F. Vancomycin (85%)

Correct

85%

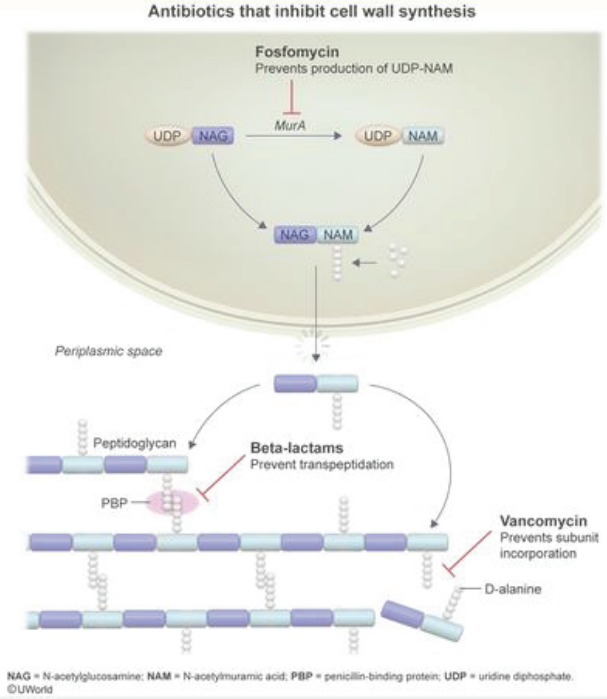
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Exhibit Display



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NAG = N-acetylglucosamine; NAM = N-acetylmuramic acid; PBP = penicillin-binding protein; UDP = uridine diphosphate.
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The bacterial cell wall is composed of cross-linked **peptidoglycan subunits** on a backbone of N-acetylmuramic acid (NAM) and N-acetylglucosamine (NAG). Because cell wall disruption results in bacterial lysis, many antibiotics target cell wall synthesis, including the following:

- **Fosfomycin** blocks development of the NAM-NAG polymer backbone by inhibiting the enzyme MurA. Resistance stems primarily from efflux pumps or alterations to MurA that prevent fosfomycin binding **(Choice B)**.

- **Vancomycin** inhibits transpeptidase from cross linking a growing peptidoglycan chain by binding to the **D-alanine–D-alanine terminus** of pentapeptide peptidoglycan subunits. **Resistance to vancomycin** stems primarily from replacement of the terminal D-alanine–D-alanine with **D-alanine–D-lactate,** which reduces vancomycin binding >1000-fold.

- **Penicillin and cephalosporins** (eg, ceftriaxone) are beta-lactam antibiotics that bind to and directly inhibit transpeptidase. Resistance stems primarily from alterations to transpeptidase that reduce beta-lactam binding or the production of enzymes (eg, penicillinase) that break down the drug **(Choices A and C)**.

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inhibit transpeptidase. Resistance stems primarily from alterations to transpeptidase that reduce beta-lactam binding or the production of enzymes (eg, penicillinase) that break down the drug **(Choices A and C)**.

(Choice D) Polymyxin binds to lipopolysaccharide, leading to disruption of the bacterial cytoplasmic membrane. It does not interfere with the bacterial cell wall.

(Choice E) Tetracycline binds to the 30S ribosomal subunit and prevents binding of aminoacyl–transfer RNAs. Resistance stems primarily from an efflux pump or alteration to the ribosome that allows translation to take place even when tetracycline is present.

Educational objective:
Vancomycin binds to the terminal D-alanine–D-alanine in bacterial pentapeptide peptidoglycan subunits, which prevents transpeptidase from binding to the pentapeptide, thereby inhibiting cell wall cross-linking. Resistance stems primarily from substitution of the terminal D-alanine with D-lactate, which prevents vancomycin binding.

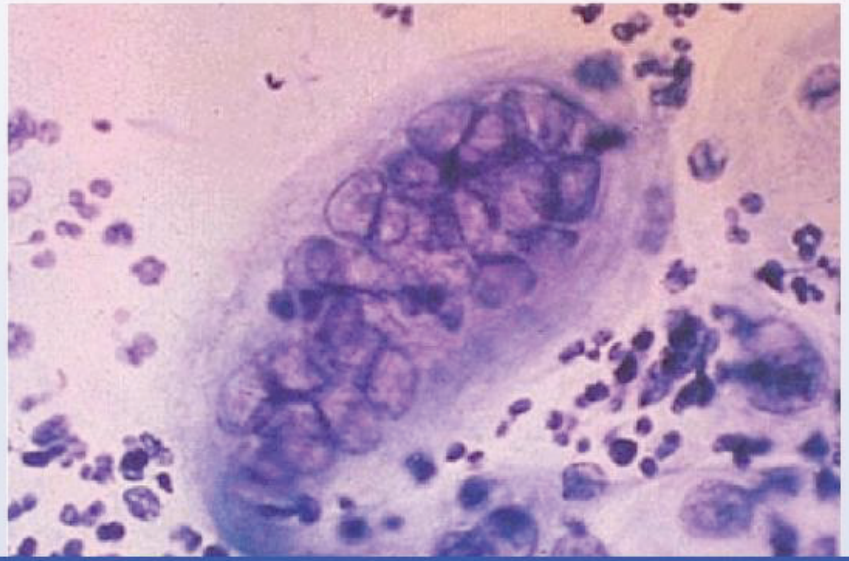
References

- Vancomycin-resistant enterococci.
- Antibiotic resistance in bacteria and its future for novel antibiotic development.

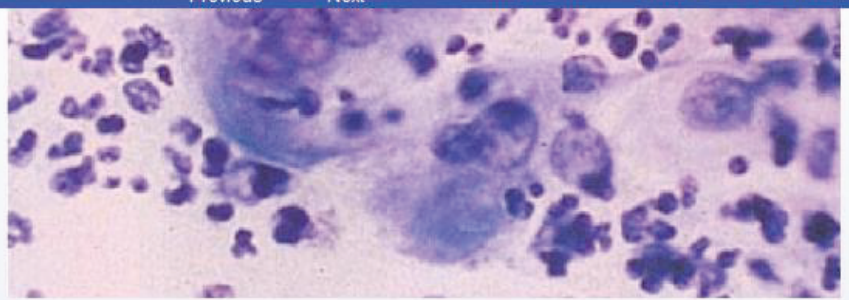
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A 4-year-old boy is brought to the office with 3 days of fever, irritability, and oral lesions. His parents are concerned due to his refusal to eat or drink and lack of urination today. Physical examination demonstrates painful ulcers on the tongue and gingiva, swollen gums, and cervical lymphadenopathy. The remainder of his examination is unremarkable. Microscopic examination of an oral ulcer base scraping is shown in the image below.



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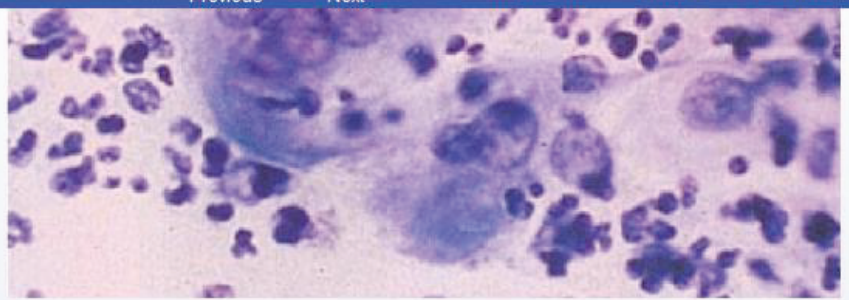


Which of the following is most likely the cause of this patient's condition?

A. Abortive infection
B. Latent infection
C. Primary infection
D. Slow virus infection
E. Virus reactivation

Submit

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Which of the following is most likely the cause of this patient's condition?

- A. ~~Abortive infection~~ (1%)
- B. Latent infection (9%)
- ✓ C. Primary infection (69%)
- D. Slow virus infection (2%)
- E. Virus reactivation (17%)

Correct

69%

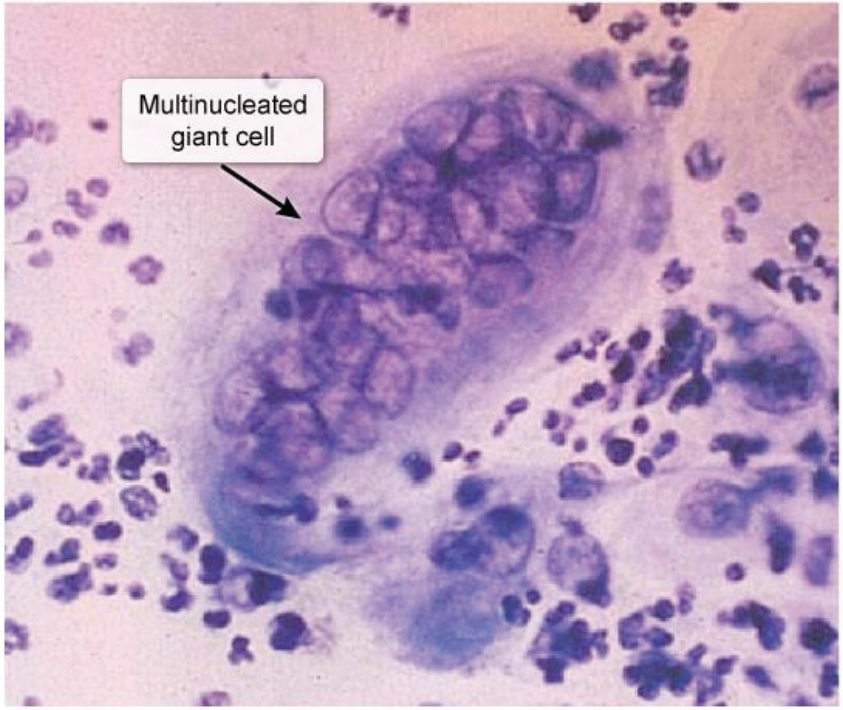
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Herpes simplex virus



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The above image depicts a **Tzanck smear**, in which epithelial cells are scraped from an ulcer base and stained. The presence of **multinucleated giant cells** is suggestive of **herpes simplex virus** (HSV) infection, which is consistent with this child's symptoms. Tzanck smears are insensitive and do not differentiate between HSV and varicella-zoster virus infection. Therefore, Tzanck smears largely have been replaced by polymerase chain reaction testing.

Primary infection with HSV-1 results in herpetic **gingivostomatitis**. Peak age for primary infection is age 6 months to 5 years. Prodromal symptoms (eg, fever, malaise, chills) begin approximately 1 week after contact with an infected person (who is generally asymptomatic). Painful **vesicles** appear, extensively covering the lips and gingiva, and may include the palate, tongue, or oropharynx. The vesicles organize into extensive ulcers and resolve within 1-2 weeks. The pain of gingivostomatitis often results in **dehydration**, the most common reason for hospitalization.

(Choice A) An abortive viral infection refers to an infection in which the virus enters the cell but does not successfully produce new infective virus. Therefore, an abortive infection is not capable of causing disease.

(Choice B) HSV is capable of latency by integrating into the trigeminal (or sacral, for HSV-2) ganglia.

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disease.

(Choice B) HSV is capable of latency by integrating into the trigeminal (or sacral, for HSV-2) ganglia. However, during latency no virus is produced and therefore no clinical disease occurs.

(Choice D) A slow virus infection is characterized by a prolonged incubation period that lasts months to years. During this time, the virus gradually multiplies before finally causing clinically apparent disease. Examples of slow viral infections include HIV, hepatitis C, and subacute sclerosing panencephalitis following measles infection.

(Choice E) Reactivation of HSV from the trigeminal ganglia causes herpes labialis. In contrast to gingivostomatitis, recurrent labialis disease is usually mild, unilateral, and limited to the lips due to host immune mechanisms (eg, presence of neutralizing antibody & HSV-specific cytotoxic T cells).

Educational objective:
Herpetic gingivostomatitis is a severe vesicular or ulcerative disease following primary infection with herpes simplex virus type 1. The diagnosis is supported by the presence of multinucleated giant cells in a Tzanck smear. Involvement of the gingiva, tongue, palate, and pharynx along with systemic symptoms (eg, fever, malaise) is common. In contrast, herpes reactivation in the trigeminal ganglia generally results in mild perioral vesicles.

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A 38-year-old woman comes to the emergency department due to abdominal discomfort and diarrhea. Her symptoms began after she returned yesterday from a Caribbean cruise. She consumed bottled water but ate raw, local seafood when visiting one of the islands. The cruise line has reported no other passengers with abdominal illness. On examination, the abdomen is soft with mild, generalized tenderness and hyperactive bowel sounds. A comma-shaped, oxidase-positive, gram-negative rod naturally found in salt water is implicated in her illness. Stool microscopy is most likely to demonstrate which of the following findings?

A. Many leukocytes, with eosinophilic predominance
B. Many leukocytes, with monocytic predominance
C. Many leukocytes, with neutrophilic predominance
D. Numerous erythrocytes and some leukocytes
E. Some mucus and no erythrocytes or leukocytes

Submit

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with abdominal illness. On examination, the abdomen is soft with mild, generalized tenderness and hyperactive bowel sounds. A comma-shaped, oxidase-positive, gram-negative rod naturally found in salt water is implicated in her illness. Stool microscopy is most likely to demonstrate which of the following findings?

A. ~~Many leukocytes, with eosinophilic predominance~~ (3%)

B. ~~Many leukocytes, with monocytic predominance~~ (5%)

C. Many leukocytes, with neutrophilic predominance (44%)

D. ~~Numerous erythrocytes and some leukocytes~~ (5%)

E. Some mucus and no erythrocytes or leukocytes (41%)

Correct

41%
Answered correctly

01 min, 47 secs
Time Spent

10/08/2020
Last Updated

Explanation

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Stool findings in acute diarrhea			
	Mechanism	**Stool findings**	**Examples of pathogens**
Watery diarrhea	Noninflammatory (enterotoxin)	No fecal leukocytes No red cells	*Vibrio cholerae*, enterotoxigenic *Escherichia coli*, *Bacillus cereus*, *Staphylococcus aureus*, some viruses, *Giardia lamblia*, *Cryptosporidium* species, *Cyclospora* species, microsporidia
Dysentery or inflammatory diarrhea	Inflammatory (invasion or cytotoxin)	Fecal polymorphonuclear leukocytes With or without red cells	*Shigella* species, *Salmonella* species, *Campylobacter jejuni*, enteroinvasive *E coli*, *Yersinia enterocolitica*, *Clostridium difficile*, *Entamoeba histolytica*

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		With or without red cells	*difficile*, *Entamoeba histolytica*
Enteric fever	Penetration & possible dissemination	Fecal mononuclear leukocytes	*Salmonella* Typhi

Vibrio cholerae is an oxidase-positive, gram-negative, comma-shaped organism that requires salt for growth and exists naturally in aquatic environments. Transmission occurs due to ingestion of contaminated food or water. Sporadic cases are often caused by the consumption of **contaminated shellfish**; outbreaks may occur in areas where safe water, sanitation, and health care services are limited.

Pathogens typically cause diarrhea by invading/damaging the intestinal epithelium or releasing enterotoxins. *V cholerae* is a noninvasive organism. It clumps together in colonies along the surface of the small intestine and causes diarrhea via the elaboration of **cholera toxin** (related to enterotoxigenic *Escherichia coli* heat-labile toxin). This enterotoxin enters intestinal epithelial cells and activates adenylate cyclase, leading to increased chloride efflux, reduced sodium reabsorption, and the subsequent movement of water from the enterocyte to the gastrointestinal lumen.

Patients typically present with **high-volume, watery diarrhea** that can cause dehydration and death within 12 hours. Because the pathogen is noninvasive and the toxin does not cause cell death, stool microscopy

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of water from the enterocyte to the gastrointestinal lumen.

Patients typically present with **high-volume, watery diarrhea** that can cause dehydration and death within 12 hours. Because the pathogen is noninvasive and the toxin does not cause cell death, stool microscopy generally reveals **no leukocytes or erythrocytes**. However, flecks of mucus are often seen (**rice-water stool**) due to the activation of goblet cells. Aggressive fluid resuscitation is the mainstay of therapy.

(Choice A) Charcot-Leyden crystals (from eosinophil breakdown) in the stool are sometimes seen in intestinal parasitic infections. Diarrhea with peripheral eosinophilia can be seen with *Strongyloides*, *Ancylostoma*, *Ascaris*, *Toxocara*, and *Trichinella* (but not with *Giardia* or *Entamoeba*).

(Choice B) The presence of leukocytes with monocytic predominance is typical for typhoid fever caused by *Salmonella* Typhi.

(Choices C and D) Invading bacteria that cause dysentery or inflammatory diarrhea (eg, *Shigella* species, *Salmonella* species, *Campylobacter jejuni*, enteroinvasive *E coli* [EIEC]) are usually marked by leukocytes with neutrophilic predominance and erythrocytes. A hemorrhagic organism (eg, enterohemorrhagic *E coli* O157:H7, which causes toxin-mediated enterocyte death and intestinal hemorrhage without mucosal invasion) would be characterized by erythrocytes without leukocytes.

Educational objective:

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(Choice B) The presence of leukocytes with monocytic predominance is typical for typhoid fever caused by *Salmonella* Typhi.

(Choices C and D) Invading bacteria that cause dysentery or inflammatory diarrhea (eg, *Shigella* species, *Salmonella* species, *Campylobacter jejuni*, enteroinvasive *E coli* [EIEC]) are usually marked by leukocytes with neutrophilic predominance and erythrocytes. A hemorrhagic organism (eg, enterohemorrhagic *E coli* O157:H7, which causes toxin-mediated enterocyte death and intestinal hemorrhage without mucosal invasion) would be characterized by erythrocytes without leukocytes.

Educational objective:

Vibrio cholerae and enterotoxigenic *Escherichia coli* cause a purely toxin-mediated watery diarrhea. The toxins secreted by these organisms modify electrolyte handling by enterocytes but do not cause cell death; therefore, no erythrocytes or leukocytes are typically noted on stool microscopy.

References

- Laboratory diagnosis of bacterial gastroenteritis.
- Complexity of rice-water stool from patients with Vibrio cholerae plays a role in the transmission of infectious diarrhea.

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A 3-month-old boy is brought to the emergency department due to 2 days of fever and irritation that progressed to lethargy. Temperature is 38.6 C (101.5 F). A lumbar puncture is performed, and the results of cerebrospinal fluid (CSF) analysis are as follows:

Glucose	30 mg/dL
Protein	180 mg/dL
Leukocytes	1,000/mm^3

Gram-negative coccobacilli are isolated from the CSF. These organisms demonstrate little growth on 5% sheep blood agar but grow well when incubated on the same media alongside colonies of *Staphylococcus aureus*. Staphylococci promote the growth of these bacteria by supplementing which of the following substances?

A. ATP

B. Catalase

C. Iron

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Leukocytes	1,000/mm^3

Gram-negative coccobacilli are isolated from the CSF. These organisms demonstrate little growth on 5% sheep blood agar but grow well when incubated on the same media alongside colonies of *Staphylococcus aureus*. Staphylococci promote the growth of these bacteria by supplementing which of the following substances?

- A. ATP
- B. Catalase
- C. Iron
- D. Lactose
- E. NAD+
- F. Pyruvate

Submit

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A 73-year-old woman comes to the emergency department with a 3-day history of worsening breathlessness and cough productive of thick, rust-colored sputum. The patient has a longstanding history of hypertension. Temperature is 38.3 C (101 F), blood pressure is 130/68 mm Hg, pulse is 102/min, and respirations are 24/min. BMI is 27 kg/m^2. Jugular venous pressure is normal and there is no lower extremity edema. Heart sounds are normal with no murmur. Lung auscultation reveals left lower lobe crackles and bronchial breath sounds. Leukocyte count is 14,000/mm^3 with 80% neutrophils and 7% bands, hemoglobin is 13.6 g/dL, and platelets are 400,000/mm^3. Serum levels of which of the following are most likely to be elevated in this patient?

A. B-type natriuretic peptide
B. Cold agglutinins
C. Prealbumin
D. Procalcitonin
E. Transferrin

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breathlessness and cough productive of thick, rust-colored sputum. The patient has a longstanding history of hypertension. Temperature is 38.3 C (101 F), blood pressure is 130/68 mm Hg, pulse is 102/min, and respirations are 24/min. BMI is 27 kg/m^2. Jugular venous pressure is normal and there is no lower extremity edema. Heart sounds are normal with no murmur. Lung auscultation reveals left lower lobe crackles and bronchial breath sounds. Leukocyte count is 14,000/mm^3 with 80% neutrophils and 7% bands, hemoglobin is 13.6 g/dL, and platelets are 400,000/mm^3. Serum levels of which of the following are most likely to be elevated in this patient?

A. B-type natriuretic peptide (11%)
B. Cold agglutinins (24%)
C. Prealbumin (10%)
D. Procalcitonin (24%)
E. Transferrin (29%)

Correct

24%

01 min, 39 secs

01/20/2021

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Acute phase reactants (APRs) are proteins whose serum concentrations change by ≥25% during periods of inflammation. Several APRs have diagnostic and prognostic utility and can be interpreted on the basis of serum concentrations:

- **Positive APRs** (serum levels rise in acute inflammatory states) include fibrinogen, C-reactive protein, ferritin, hepcidin, ceruloplasmin, haptoglobin, von Willebrand factor, and complement. The erythrocyte sedimentation rate (the time required for erythrocytes to settle from suspension) is an indirect measure of positive APRs.
- **Negative APRs** (serum levels fall in acute inflammatory states) include albumin, transferrin, and transthyretin (prealbumin).

Procalcitonin, a precursor of calcitonin produced by monocytes and the C cells of the thyroid, is a unique APR that has positive and negative properties. Levels **rise** in response to **bacterial toxins** and **fall** in response to **viral infections**, and therefore levels can suggest the etiology of community-acquired pneumonia. This patient has lobar pneumonia manifesting with fever, rust-colored sputum, and neutrophil-predominant leukocytosis, likely due to a bacterial infection (eg, *Streptococcus pneumoniae*). Therefore, procalcitonin levels are expected to be elevated.

(Choice A) B-type natriuretic peptide is secreted by the ventricles in response to elevated ventricular filling

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(Choice A) B-type natriuretic peptide is secreted by the ventricles in response to elevated ventricular filling pressure, which is seen in decompensated heart failure. Patients with heart failure often have elevated jugular venous pressure and lower extremity edema, pulmonary examination findings are usually bilateral, and fevers and leukocytosis would not be expected.

(Choice B) Cold agglutinins (ie, IgM against erythrocyte I antigen) are nonspecific but often seen in patients with *Mycoplasma pneumoniae*. However, patients with *M pneumoniae* typically present with a dry cough and pharyngitis, and laboratory results demonstrate a mild hemolytic anemia with a normal leukocyte count. When pneumonia occurs due to *M pneumoniae*, examination findings are characteristically scattered and bilateral.

(Choices C and E) Prealbumin (transthyretin) and transferrin are negative APRs and would be decreased in this acutely ill patient. Prealbumin levels are also decreased in cases of malnutrition and may be helpful in evaluation of nutritional status. Transferrin is also used to determine iron status.

Educational objective:
Acute phase reactants (APRs) are proteins whose serum concentrations change by ≥25% during periods of inflammation. Procalcitonin is a unique APR that can rise or fall depending on the etiology of the infection; elevated levels correlate with a bacterial source, whereas low levels indicate a viral source.

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(Choice B) Cold agglutinins (ie, IgM against erythrocyte I antigen) are nonspecific but often seen in patients with *Mycoplasma pneumoniae*. However, patients with *M pneumoniae* typically present with a dry cough and pharyngitis, and laboratory results demonstrate a mild hemolytic anemia with a normal leukocyte count. When pneumonia occurs due to *M pneumoniae*, examination findings are characteristically scattered and bilateral.

(Choices C and E) Prealbumin (transthyretin) and transferrin are negative APRs and would be decreased in this acutely ill patient. Prealbumin levels are also decreased in cases of malnutrition and may be helpful in evaluation of nutritional status. Transferrin is also used to determine iron status.

Educational objective:

Acute phase reactants (APRs) are proteins whose serum concentrations change by ≥25% during periods of inflammation. Procalcitonin is a unique APR that can rise or fall depending on the etiology of the infection; elevated levels correlate with a bacterial source, whereas low levels indicate a viral source.

References

- Role of procalcitonin in guiding antibiotic therapy.

Pathology Infectious Diseases Community acquired pneumonia

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A 47-year-old man comes to the emergency department due to fever and fatigue. He has a history of HIV and has not been taking his antiretrovirals consistently. His temperature is 38.3 C (100.9 F), blood pressure is 110/70 mm Hg, pulse is 104/min, and respirations are 20/min. Physical examination is notable for hepatosplenomegaly and multiple erythematous papules. Laboratory studies show pancytopenia. *Histoplasma* antigen testing is positive. Intravenous amphotericin B therapy is initiated for disseminated histoplasmosis. A day later, the patient develops palpitations and weakness. An ECG reveals frequent premature ventricular beats. If these new signs and symptoms are caused by drug toxicity, they are most likely related to which of the following?

A. Bone marrow suppression
B. Cardiac muscle cell damage
C. Hepatocyte necrosis
D. Pulmonary hypertension
E. Renal tubular dysfunction

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and has not been taking his antiretrovirals consistently. His temperature is 38.3 C (100.9 F), blood pressure is 110/70 mm Hg, pulse is 104/min, and respirations are 20/min. Physical examination is notable for hepatosplenomegaly and multiple erythematous papules. Laboratory studies show pancytopenia. *Histoplasma* antigen testing is positive. Intravenous amphotericin B therapy is initiated for disseminated histoplasmosis. A day later, the patient develops palpitations and weakness. An ECG reveals frequent premature ventricular beats. If these new signs and symptoms are caused by drug toxicity, they are most likely related to which of the following?

A. Bone marrow suppression (3%)
B. Cardiac muscle cell damage (19%)
C. Hepatocyte necrosis (5%)
D. Pulmonary hypertension (2%)
✓ E. Renal tubular dysfunction (70%)

Correct
70%
34 secs
10/03/2020

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This patient with HIV has fever, fatigue, hepatosplenomegaly, skin lesions, and pancytopenia; these are consistent with disseminated histoplasmosis, as evidenced by the positive *Histoplasma* antigen test. **Amphotericin B** is the drug of choice to treat many systemic mycoses. It is also the most toxic antifungal medication.

The most dangerous adverse effect of amphotericin B is its **nephrotoxicity**; this is due to both a decrease in glomerular filtration rate and direct toxic effects on the tubular epithelium. Nephrotoxicity can lead to anemia (decreased erythropoietin production) and electrolyte abnormalities. **Hypokalemia** and (less often) hypomagnesemia are common due to an increase in the membrane permeability of the distal tubule. Hypokalemia can cause **weakness** and **arrhythmias**. ECG findings in hypokalemia include T wave flattening, ST-segment depression, prominent U waves, and premature atrial and ventricular contractions. Profound hypokalemia can cause ventricular tachycardia or fibrillation.

(Choice A) Bone marrow suppression is associated with many chemotherapeutic agents, chloramphenicol, zidovudine, and gold-containing medications. Bone marrow suppression would not cause ECG changes.

(Choice B) Doxorubicin and daunorubicin are associated with irreversible dose-dependent cardiotoxicity, which is not a side effect of amphotericin B.

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Profound hypokalemia can cause ventricular tachycardia or fibrillation.

(Choice A) Bone marrow suppression is associated with many chemotherapeutic agents, chloramphenicol, zidovudine, and gold-containing medications. Bone marrow suppression would not cause ECG changes.

(Choice B) Doxorubicin and daunorubicin are associated with irreversible dose-dependent cardiotoxicity, which is not a side effect of amphotericin B.

(Choice C) Acetaminophen and halothane are examples of medications that can cause liver necrosis. Amphotericin B can lead to liver toxicity, not necrosis. Arrhythmias and palpitations are more likely caused by electrolyte abnormalities due to renal tubular dysfunction.

(Choice D) Busulfan and bleomycin are examples of drugs that cause pulmonary fibrosis and can lead to pulmonary hypertension.

Educational objective:
Hypokalemia and hypomagnesemia are common electrolyte disturbances in patients undergoing treatment with amphotericin B and reflect an increase in distal tubular membrane permeability.

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A 29-year-old man is hospitalized due to a flulike illness. His symptoms abruptly began 3 days ago with fever, rigors, malaise, headache, and myalgia. The patient has no prior health conditions and is usually very active, participating in multiple outdoor sports. Temperature is 38.9 C (102 F), blood pressure is 124/84 mm Hg, and pulse is 110/min. Physical examination shows an ill-appearing man with bilateral conjunctival suffusion. Lung and heart sounds are normal, but abdominal examination reveals mild hepatosplenomegaly. Generalized lymphadenopathy is also present. A test for influenza antigen is negative, and blood cultures in routine growth media are negative. The patient subsequently develops progressive jaundice and renal failure. Further testing detects an infection with a highly motile, corkscrew-shaped pathogen. This patient most likely acquired the infection via which of the following?

A. Being in close vicinity of infected bats
B. Bites from infected rodent fleas
C. Exposure to water contaminated with animal urine
D. Hiking in tick-infested wooded areas
E. Hunting and skinning of wild rabbits

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fever, rigors, malaise, headache, and myalgia. The patient has no prior health conditions and is usually very active, participating in multiple outdoor sports. Temperature is 38.9 C (102 F), blood pressure is 124/84 mm Hg, and pulse is 110/min. Physical examination shows an ill-appearing man with bilateral conjunctival suffusion. Lung and heart sounds are normal, but abdominal examination reveals mild hepatosplenomegaly. Generalized lymphadenopathy is also present. A test for influenza antigen is negative, and blood cultures in routine growth media are negative. The patient subsequently develops progressive jaundice and renal failure. Further testing detects an infection with a highly motile, corkscrew-shaped pathogen. This patient most likely acquired the infection via which of the following?

A. Being in close vicinity of infected bats (2%)
B. Bites from infected rodent fleas (3%)
✓ C. Exposure to water contaminated with animal urine (73%)
D. Hiking in tick-infested wooded areas (15%)
E. Hunting and skinning of wild rabbits (4%)

73%
01 min, 46 secs
02/06/2021

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Leptospirosis is a widespread, zoonotic infection caused by several species of *Leptospira*, a thin, highly coiled, **motile spirochete** that infects wild (eg, rodents) and domestic (eg, dogs, cattle) animals. Infected animals harbor the organism in the proximal renal tubule and excrete it in urine. Transmission to humans primarily occurs during outdoor recreational (eg, kayaking, freshwater swimming) or occupational activities that exposes them to **water contaminated with animal urine**.

Most cases of leptospirosis are mild or subclinical. However, some patients develop a **flu-like illness** (eg, fever, rigors, myalgia, headache), lymphadenopathy, or more severe end-organ disease such as renal failure or hepatic failure (eg, jaundice, hepatomegaly). **Conjunctival suffusion**, redness of the conjunctiva that resembles conjunctivitis but is noninflammatory, is an important diagnostic clue. Because spirochetes do not grow well on traditional culture media, initial testing (eg, influenza antigen, blood culture) is often negative. However, specialized culture media can often identify the **corkscrew-shaped organism**. Most cases are self-limited and do not require treatment.

(Choice A) Bats can transmit rabies to humans via a bite wound. Manifestations typically begin with flulike symptoms and progress to fever, hydrophobia, pharyngeal spasms, coma, and death. Rabies is a cylindrical, enveloped RNA virus; it is not a motile, corkscrew-shaped organism.

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(Choice B) *Yersinia*, a bacteria transmitted by animal (eg, rodent) fleas, can cause bubonic plague, which typically presents with sudden-onset, flulike symptoms followed by intense pain and regional lymphadenopathy (eg, inguinal). *Yersinia* grows well on traditional culture media; it appears on Gram stain as a gram-negative coccobacillus.

(Choice D) Rocky Mountain spotted fever is a tickborne illness caused by the small, gram-negative bacterium *Rickettsia rickettsii*. Although initial symptoms are often flulike and may include conjunctivitis, most individuals develop an erythematous rash that begins on the wrists and ankles, spreads to the center of the body, and includes the palms and soles. The organism is not corkscrew-shaped.

(Choice E) Tularemia is caused by the gram-negative bacterium *Francisella tularensis*, which frequently infects rabbits. Manifestations typically include flulike symptoms followed by lymphadenopathy and a papulo-ulcerative eschar at the site of inoculation.

Educational objective:
Leptospirosis is a zoonotic infection caused by the motile spirochete *Leptospira*. Transmission primarily occurs when humans come into contact with water contaminated with animal urine during outdoor recreational or occupational activities. Patients classically have a mild, self-limited, flulike illness but may develop more serious complications such as renal or hepatic failure.

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A 16-year-old boy comes to the office due to 3 days of burning with urination and yellow penile discharge. The patient is sexually active with one female partner; they engage in vaginal intercourse and do not use condoms. He has no other medical conditions, takes no medications, and has no allergies. Urine nucleic acid amplification test results are pending, and urethral Gram stain is shown in the exhibit. Approprate treatment of this patient's condition involves antibiotics from which of the following drug classes?

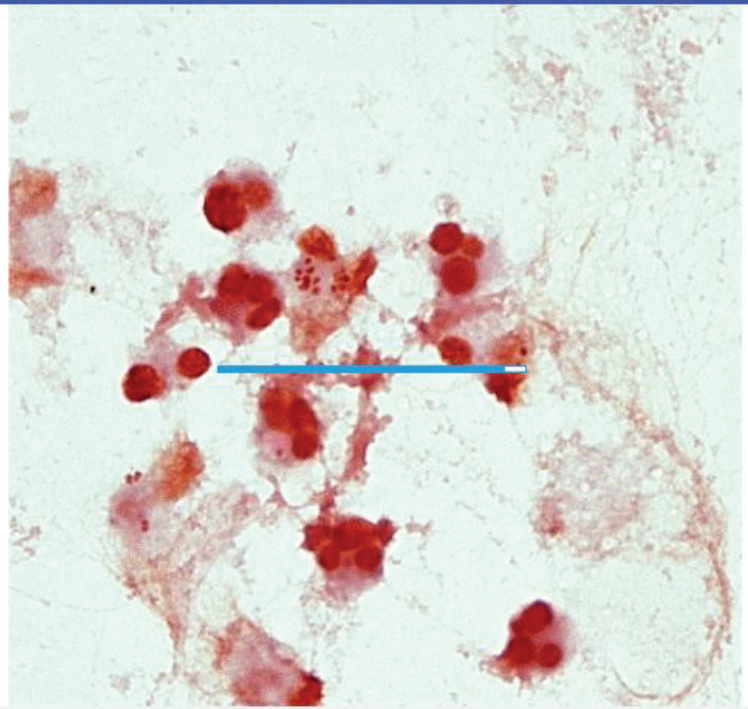
- A. Fluoroquinolone and macrolide
- B. Fluoroquinolone and third-generation cephalosporin
- C. Macrolide only
- D. Penicillin only
- E. Tetracycline and third-generation cephalosporin
- F. Third-generation cephalosporin only

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Exhibit Display



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A 16-year-old boy comes to the office due to 3 days of burning with urination and yellow penile discharge. The patient is sexually active with one female partner; they engage in vaginal intercourse and do not use condoms. He has no other medical conditions, takes no medications, and has no allergies. Urine nucleic acid amplification test results are pending, and urethral Gram stain is shown in the exhibit. Approprate treatment of this patient's condition involves antibiotics from which of the following drug classes?

- A. Fluoroquinolone and macrolide (4%)
- B. Fluoroquinolone and third-generation cephalosporin (9%)
- C. Macrolide only (2%)
- D. Penicillin only (1%)
- ✓ E. Tetracycline and third-generation cephalosporin (75%)
- ✗ F. Third-generation cephalosporin only (5%)

Incorrect
Correct answer

75%
Answered correctly

01 min, 26 secs
Time Spent

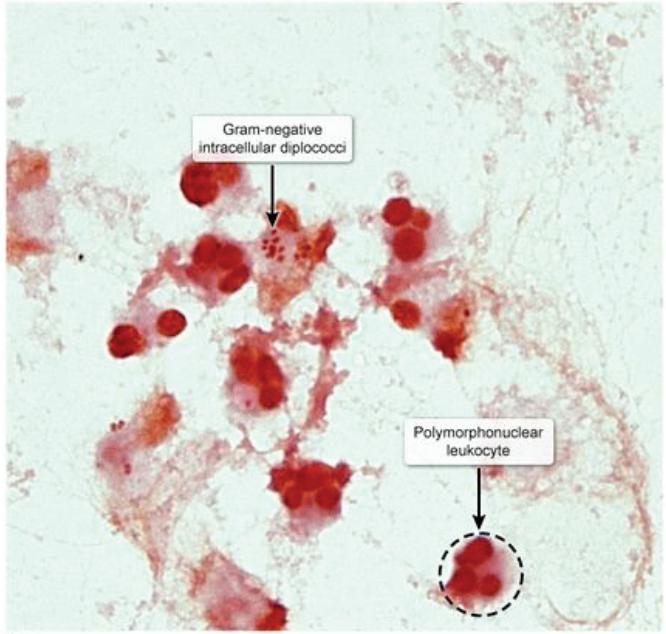
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Exhibit Display

Neisseria gonorrhoeae



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This patient with dysuria and penile discharge likely has **infectious urethritis** due to sexually transmitted infection. Most cases are caused by *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or *Mycoplasma genitalium*. The underlying pathogen is typically identified with **nucleic acid amplification testing** (NAAT) of urine, vaginal, or endocervical swab. However, light microscopy with **Gram stain** can be performed to rapidly identify *N gonorrhoeae* while awaiting NAAT results, as follows:

- **Gonococcal urethritis:** leukocytes with **intracellular gram-negative diplococci**
- **Nongonococcal urethritis:** leukocytes with no visible organisms; because *Chlamydia* and *Mycoplasma* do not have sufficient peptidoglycan in the cell wall to take up Gram stain, they cannot be ruled in or out with microscopy

Patients with gonococcal urethritis who have coinfection with *C trachomatis* or **uncertain *C trachomatis* status** (as in this patient whose NAAT results are pending) require a **third-generation cephalosporin** (eg, ceftriaxone) and a **tetracycline** (eg, doxycycline) to cover gonococcus and possible *C trachomatis* coinfection. Patients with gonococcal urethritis who have negative *C trachomatis* NAAT should be treated with third-generation cephalosporin (eg, ceftriaxone) alone **(Choice F)**. Patients with nongonococcal urethritis should be treated with macrolide (eg, azithromycin) or tetracycline (eg, doxycycline) monotherapy **(Choice C)**.

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(Choices A and B) *N gonorrhoeae* is largely resistant to fluoroquinolones (eg, ciprofloxacin, levofloxacin), so this class of medication is not recommended.

(Choice D) Penicillin is the treatment of choice for syphilis. However, empiric treatment is not recommended unless a chancre is present. Other stages of syphilis should only be treated when serology (eg, rapid plasma reagin, VDRL) is positive or the organism is otherwise identified.

Educational objective:

Infectious urethritis in men is typically caused by *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or *Mycoplasma genitalium*. Diagnosis is generally made by nucleic acid amplification testing, but microscopy with Gram stain can be used to quickly diagnose gonococcal infection. Patients with gonorrhea and positive or uncertain *Chlamydia* status require ceftriaxone and doxycycline; ceftriaxone alone can be used in those who do not have *Chlamydia* coinfection.

References

- Management of gonorrhea in adolescents and adults in the United States.

Pharmacology	Infectious Diseases	Urethritis
Subject	System	Topic

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Exhibit Display



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A 3-month-old boy is brought to the emergency department due to 2 days of fever and irritation that progressed to lethargy. Temperature is 38.6 C (101.5 F). A lumbar puncture is performed, and the results of cerebrospinal fluid (CSF) analysis are as follows:

Glucose	30 mg/dL
Protein	180 mg/dL
Leukocytes	1,000/mm^3

Gram-negative coccobacilli are isolated from the CSF. These organisms demonstrate little growth on 5% sheep blood agar but grow well when incubated on the same media alongside colonies of *Staphylococcus aureus*. Staphylococci promote the growth of these bacteria by supplementing which of the following substances?

A. ATP
B. Catalase
C. Iron

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Leukocytes	1,000/mm^3

Gram-negative coccobacilli are isolated from the CSF. These organisms demonstrate little growth on 5% sheep blood agar but grow well when incubated on the same media alongside colonies of *Staphylococcus aureus*. Staphylococci promote the growth of these bacteria by supplementing which of the following substances?

- A. ATP
- B. Catalase
- C. Iron
- D. Lactose
- E. NAD+
- F. Pyruvate

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Leukocytes 1,000/mm³

Gram-negative coccobacilli are isolated from the CSF. These organisms demonstrate little growth on 5% sheep blood agar but grow well when incubated on the same media alongside colonies of *Staphylococcus aureus*. Staphylococci promote the growth of these bacteria by supplementing which of the following substances?

- A. ATP (3%)
- B. Catalase (25%)
- C. Iron (7%)
- D. Lactose (2%)
- E. NAD+ (59%)
- F. Pyruvate (1%)

Incorrect
Correct answer

59%

01 min, 40 secs

01/30/2021

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This patient likely has *Haemophilus influenzae* type b meningitis (which may occur in patients who are unvaccinated or immunocompromised). ***Haemophilus*** (from the Greek for blood-loving) requires both **X factor** (hematin) and **V factor** (NAD+) to support growth. Sheep blood agar does not allow *Haemophilus* growth due to insufficient nutrients and the V factor-inactivating enzymes in the medium.

Growth of *Haemophilus* species on sheep blood agar can be achieved by cross-streaking the medium with *Staphylococcus aureus*. *H influenzae* colonies will grow around the streaks of β-hemolytic *S aureus* colonies because the latter actively secrete **V factor (NAD+)** into the medium and facilitate release of additional X factor (hematin) from β-hemolysis-induced erythrocyte lysis. This is known as the "satellite" phenomenon.

(Choices A and F) Pyruvate is the end product of glycolysis and is a starting substrate for the synthesis of glucose, lactate, fatty acids, amino acids, and nucleic acids. Bacteria use pyruvate in the metabolism of sugars for energy in the form of ATP.

(Choice B) Catalase is an enzyme present in staphylococci; the presence or absence of this enzyme is used to differentiate staphylococci from streptococci.

(Choice C) Iron is an essential growth factor for many bacteria, and it is provided in all blood agars from the iron within erythrocytes

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(Choice B) Catalase is an enzyme present in staphylococci; the presence or absence of this enzyme is used to differentiate staphylococci from streptococci.

(Choice C) Iron is an essential growth factor for many bacteria, and it is provided in all blood agars from the iron within erythrocytes.

(Choice D) The use of lactose fermentation as a source of energy is best known in *Escherichia coli* with the well studied *lac* operon, an inducible and repressible genetic sequence coding for the enzymes necessary for lactose fermentation in the absence of glucose. It is activated by a sensed glucose deficit and repressed when glucose is available again.

Educational objective:
Haemophilus influenzae is a "blood-loving" organism that requires X (hematin) and V (NAD+) factors for growth. This can be accomplished by growing *H influenzae* in the presence of *Staphylococcus aureus* and demonstrating the "satellite phenomenon," whereby *H influenzae* grow only near the β-hemolytic *S aureus* colonies that produce the needed X and V factors.

Microbiology	Infectious Diseases	Haemophilus influenzae
Subject	System	Topic

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A 45-year-old woman is hospitalized due to severe *Pneumocystis* pneumonia. The patient has a history of injection drug use and was diagnosed with HIV 10 years ago. She does not adhere to antiretroviral therapy and has developed resistance to multiple antiretroviral medications. Laboratory evaluation reveals severe immunosuppression with a high HIV viral load. After the patient is adequately treated for pneumonia, HIV genotypic analysis is performed. The viral isolates are found to have a mutation in the variable (V3) region of the *env* gene, which makes the virus capable of infecting T cells with a specific surface receptor, but infection of macrophages is inefficient. Which of the following antiretroviral medications is most likely to be ineffective in this patient?

A. Atazanavir
B. Efavirenz
C. Enfuvirtide
D. Maraviroc
E. Raltegravir
F. Tenofovir

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and has developed resistance to multiple antiretroviral medications. Laboratory evaluation reveals severe immunosuppression with a high HIV viral load. After the patient is adequately treated for pneumonia, HIV genotypic analysis is performed. The viral isolates are found to have a mutation in the variable (V3) region of the *env* gene, which makes the virus capable of infecting T cells with a specific surface receptor, but infection of macrophages is inefficient. Which of the following antiretroviral medications is most likely to be ineffective in this patient?

A. Atazanavir (2%)
B. Efavirenz (5%)
C. Enfuvirtide (22%)
D. Maraviroc (59%)
E. Raltegravir (4%)
F. Tenofovir (5%)

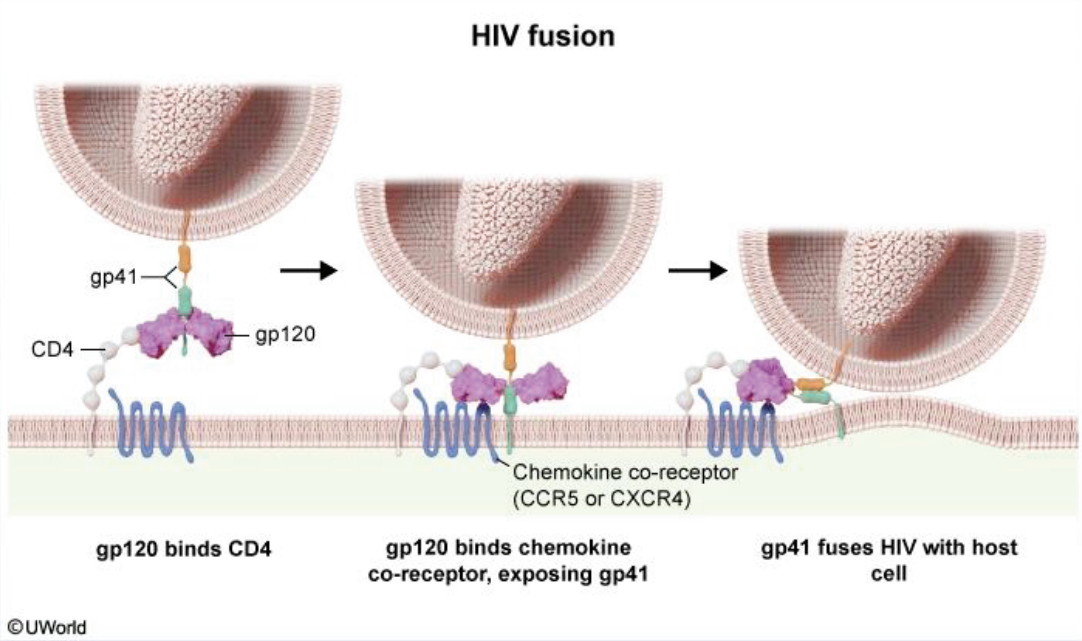
Correct

59%

54 secs

12/15/2020

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HIV binds to host cells using the host CD4 receptor and a chemokine coreceptor (either CCR5 or CXCR4). The virus preferentially targets T lymphocytes, dendritic cells, and macrophages because these cells contain high surface concentrations of CD4. However, each of these cell types contains different surface

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HIV binds to host cells using the host CD4 receptor and a chemokine coreceptor (either CCR5 or CXCR4). The virus preferentially targets T lymphocytes, dendritic cells, and macrophages because these cells contain high surface concentrations of CD4. However, each of these cell types contains different surface concentrations of the 2 chemokine receptors. HIV is considered **tropic** for a certain cell type, depending on whether it preferentially binds to CCR5 or CXCR4 for viral entry, as follows:

- **R5 virus** uses CCR5 for viral entry and is considered **macrophage-tropic** because CCR5 is expressed in high concentrations on both macrophages and lymphocytes. R5 is the predominant HIV type.
- **X4 virus** uses CXCR4 for viral entry and is considered **T lymphotropic** because CXCR4 is expressed primarily on T lymphocytes but only **minimally on macrophages**.

HIV trophism is determined by a gene sequence in the variable (V3) region of the ***env* gene**, which encodes for the HIV surface glycoprotein 120. This glycoprotein mediates viral attachment to the CD4 receptor and chemokine coreceptor.

The laboratory results in this case indicate an X4 virus (T lymphotropic with minimal macrophage invasion). Patients with X4 virus cannot be treated with HIV medications that target CCR5 (eg, **maraviroc**)

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receptor and chemokine coreceptor.

The laboratory results in this case indicate an X4 virus (T lymphotropic with minimal macrophage invasion). Patients with X4 virus cannot be treated with HIV medications that target CCR5 (eg, **maraviroc**) because the X4 virus uses CXCR4, not CCR5, to enter cells.

(Choice A) Protease inhibitors (eg, atazanavir, indinavir, darunavir) inhibit HIV protease from cleaving HIV polyproteins into the individual, functional proteins that compose the virus. This results in the formation of immature, noninfectious virions that are unable to infect T cells or macrophages.

(Choices B and F) Non-nucleoside reverse transcriptase inhibitors (eg, efavirenz, nevirapine) allosterically bind reverse transcriptase, which alters its shape and prevents it from converting the HIV RNA genome into complementary DNA (cDNA). Nucleoside reverse transcriptase inhibitors (eg, tenofovir, emtricitabine) competitively bind reverse transcriptase and are integrated into growing cDNA strands, which results in chain termination. Both of these HIV medication classes truncate viral replication but do not affect viral attachment or fusion.

(Choice C) Enfuvirtide is an HIV fusion inhibitor that binds to the HIV transmembrane surface protein glycoprotein 41 and prevents the virus from fusing with the host cell membrane. Fusion inhibitors would inhibit the ability of HIV to invade both lymphocytes and macrophages.

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chain termination. Both of these HIV medication classes truncate viral replication but do not affect viral attachment or fusion.

(Choice C) Enfuvirtide is an HIV fusion inhibitor that binds to the HIV transmembrane surface protein glycoprotein 41 and prevents the virus from fusing with the host cell membrane. Fusion inhibitors would inhibit the ability of HIV to invade both lymphocytes and macrophages.

(Choice E) Integrase inhibitors (eg, raltegravir, dolutegravir) prevent the HIV enzyme integrase from incorporating viral cDNA into the host chromosome, which prevents viral replication. They do not affect viral attachment or fusion.

Educational objective:
R5 strains (macrophage-tropic) of HIV attach to the host CD4 receptor and CCR5 chemokine coreceptor; CCR5 inhibitors such as maraviroc can be used in the treatment of R5 virus. X4 strains (T lymphotropic) of HIV bind to the CD4 receptor and CXCR4 chemokine receptor; X4 virus cannot be treated with CCR5 inhibitors.

Pharmacology	Infectious Diseases	HIV
Subject	System	Topic

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A 5-year-old child is brought to the emergency department due to difficulty breathing and a low-grade fever. The patient's family recently moved to the United States from rural Nepal. Temperature is 38.1 C (100.6 F). Physical examination shows a grayish pharyngeal exudate, enlarged cervical lymph nodes, and partial soft palate paralysis. A sample of the pharyngeal exudate is obtained by oropharyngeal swab. Bacteria isolated from the exudate demonstrate exotoxin production in the laboratory. Which of the following best describes the mechanism of action of the exotoxin?

A. Autoimmune activation by antigenic mimicry
B. Degradation of lecithin
C. Inactivation of the 60S ribosomal subunit
D. Increased sensitivity to histamine
E. Intracellular protein ribosylation

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A 5-year-old child is brought to the emergency department due to difficulty breathing and a low-grade fever. The patient's family recently moved to the United States from rural Nepal. Temperature is 38.1 C (100.6 F). Physical examination shows a grayish pharyngeal exudate, enlarged cervical lymph nodes, and partial soft palate paralysis. A sample of the pharyngeal exudate is obtained by oropharyngeal swab. Bacteria isolated from the exudate demonstrate exotoxin production in the laboratory. Which of the following best describes the mechanism of action of the exotoxin?

A. ~~Autoimmune activation by antigenic mimicry~~ (5%)
B. ~~Degradation of lecithin~~ (4%)
C. Inactivation of the 60S ribosomal subunit (17%)
D. ~~Increased sensitivity to histamine~~ (0%)
✓ E. Intracellular protein ribosylation (72%)

Correct

72% Answered correctly
01 min, 10 secs Time Spent
10/25/2020 Last Updated

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Diphtheria	
Epidemiology	• Endemic in developing countries due to inadequate vaccination but rare in developed countries
Microbiology/ pathogenesis	• ***Corynebacterium diphtheriae*** colonize respiratory tract & secrete diphtheria toxin, the primary virulence factor • **Diphtheria toxin** is an AB exotoxin that inhibits protein synthesis by ADP-ribosylation of EF-2 • Toxin acts locally, causing respiratory cell necrosis with formation of fibrinous, coagulative exudates
Clinical symptoms	• Sore throat • Fever • Cervical adenopathy • Pharyngeal exudates/**coalescing pseudomembrane**
Complications	• Submucosal edema & pseudomembrane aspiration can obstruct respiratory tract, causing **suffocation** • Systemically absorbed diphtheria toxin has predilection for brain & heart tissue ○ **Myocarditis/heart failure** ○ **Neurologic toxicity**

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	○ **Neurologic toxicity**

EF-2 = elongation factor-2.

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This child has **diphtheria**, a disease caused by *Corynebacterium diphtheriae* and now rarely seen in most countries as a result of vaccination. The A (active) subunit of the diphtheria AB **exotoxin** transfers a ribose residue from NAD to a histidine on **elongation factor-2** (EF-2). The EF-2 protein is essential for peptide chain translocation on the ribosome in the process of translation. **Ribosylation** inactivates EF-2, thereby inhibiting protein synthesis and causing cell death.

(Choice A) Group A *Streptococcus* (GAS) pharyngitis can lead to rheumatic fever via antigenic mimicry. GAS and cardiac myocytes have similar antigenic protein sequences. Therefore, when the immune system mounts a response against GAS, it may also cause myocarditis and valve destruction over time. GAS pharyngitis is not typically due to exotoxins and does not classically cause local neuropathies (eg, soft palate paralysis).

(Choice B) Lecithinase (also known as phospholipase C, or *Clostridium perfringens* alpha-toxin) is the exotoxin released by *C perfringens*. This enzyme degrades membrane phospholipids (including lecithin), leading to cell membrane destruction and cell death. *C perfringens* causes gas gangrene.

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exotoxin released by *C perfringens*. This enzyme degrades membrane phospholipids (including lecithin), leading to cell membrane destruction and cell death. *C perfringens* causes gas gangrene.

(Choice C) The shiga toxin of *Shigella* and the shigalike toxin of enterohemorrhagic *Escherichia coli* (EHEC) cause inactivation of the 60S ribosomal subunit. By contrast, diphtheria toxin inactivates EF-2, not the ribosome itself. *Shigella* and EHEC cause diarrheal illnesses.

(Choice D) Pertussis toxin is an AB exotoxin released by *Bordetella pertussis* that catalyzes ribosylation of G protein α_i subunits. This results in increased cAMP production, which leads to increased insulin production, lymphocyte and neutrophil dysfunction, and increased sensitivity to histamine. Classic pertussis has a catarrhal stage (mild upper respiratory symptoms), a paroxysmal stage (whooping cough), and a convalescent stage.

Educational objective:
Diphtheria toxin is an AB exotoxin that ribosylates and inactivates elongation factor-2. This action inhibits protein synthesis and ultimately leads to cell death.

Microbiology	Infectious Diseases	Diphtheria
Subject	System	Topic

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Researchers studying fungal pathogens isolated an ergosterol biosynthetic gene by polymerase chain reaction. Using homologous recombination, they then developed a new strain of *Candida* with a mutated allele for that gene. The mutant strain was cultured in the presence of several different antifungal agents. Compared to isolates from the wild-type strain, isolates from the mutant *Candida* strain exhibited enhanced growth in the presence of drug X. Further investigation revealed that the mechanism of resistance to drug X was a decrease in ergosterol incorporation into the cell membrane. Based on this data, drug X is likely to be most closely related to which of the following antifungal agents?

A. Caspofungin
B. Cyclosporine
C. Flucytosine
D. Griseofulvin
E. Nystatin

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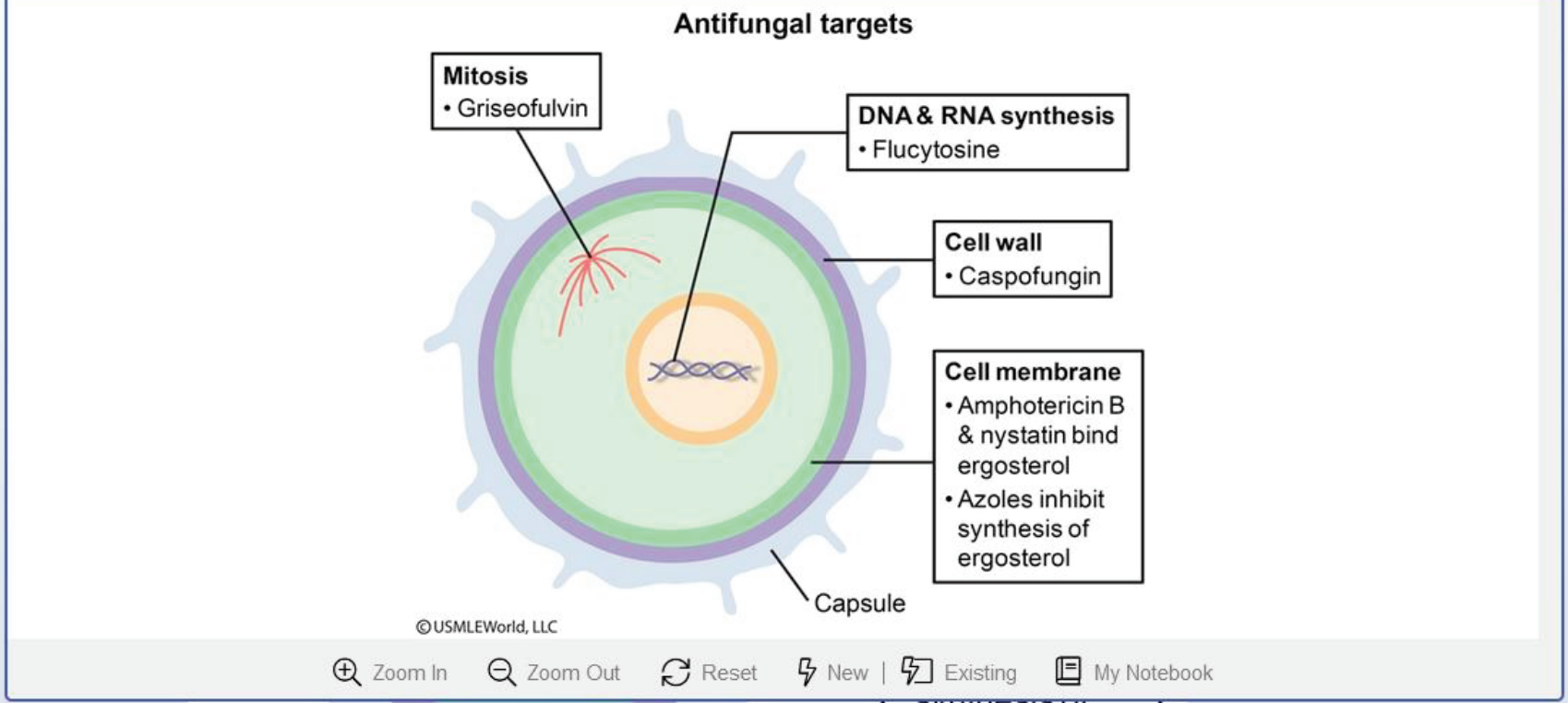
Researchers studying fungal pathogens isolated an ergosterol biosynthetic gene by polymerase chain reaction. Using homologous recombination, they then developed a new strain of *Candida* with a mutated allele for that gene. The mutant strain was cultured in the presence of several different antifungal agents. Compared to isolates from the wild-type strain, isolates from the mutant *Candida* strain exhibited enhanced growth in the presence of drug X. Further investigation revealed that the mechanism of resistance to drug X was a decrease in ergosterol incorporation into the cell membrane. Based on this data, drug X is likely to be most closely related to which of the following antifungal agents?

A. Caspofungin (22%)
B. Cyclosporine (2%)
C. Flucytosine (8%)
D. Griseofulvin (9%)
✓ E. Nystatin (57%)

57%
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11/15/2020

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Capsule

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The main classes of antifungal medications currently in use include:

1. **Polyenes** (eg, amphotericin B, nystatin): Bind to ergosterol molecules in fungal cell membranes, creating pores and causing cell lysis
2. **Triazoles** (eg, ketoconazole, fluconazole, itraconazole, voriconazole): Inhibit the synthesis of ergosterol
3. **Echinocandins** (eg, caspofungin, micafungin): Inhibit the synthesis of glucan, a component of the fungal cell wall
4. **Pyrimidines**: Flucytosine, the only agent in this class of antifungals, is converted to 5-fluorouracil within the fungal cell and interferes with fungal RNA and protein synthesis.

Of these agents, only the polyenes (amphotericin B, nystatin) depend on the amount of **ergosterol** incorporated into fungal cell membranes for their efficacy. These drugs bind to ergosterol molecules, forming **pores** in the membrane and allowing leakage of ions (especially K^+) from the cells. This disruption of cell membrane integrity leads to cell lysis. An organism that decreases the amount of ergosterol in its cell membrane would likely become resistant to polyenes. **Amphotericin** B is a systemic antifungal active against *Candida, Aspergillus, Cryptococcus, Histoplasma, Blastomyces*, and *Coccidioides*. **Nystatin** is

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of cell membrane integrity leads to cell lysis. An organism that decreases the amount of ergosterol in its cell membrane would likely become resistant to polyenes. **Amphotericin** B is a systemic antifungal active against *Candida, Aspergillus, Cryptococcus, Histoplasma, Blastomyces*, and *Coccidioides*. **Nystatin** is used topically; oral candidiasis is the main indication for its use ("swish and swallow").

(Choice A) Caspofungin is an antifungal agent that blocks synthesis of the glucan component of the fungal cell wall. It is active against *Candida* and *Aspergillus*. Caspofungin does not bind ergosterol.

(Choice B) Cyclosporine is an immunosuppressant used in transplant recipients to prevent rejection. It decreases the synthesis of IL-2, thereby inhibiting T cell proliferation.

(Choice C) Flucytosine is used in combination with amphotericin B primarily for the treatment of cryptococcal meningitis in patients with HIV. It is a nucleotide analog that competitively inhibits RNA synthesis in fungal cells.

(Choice D) Griseofulvin interacts with fungal cell microtubules, inhibiting mitosis. It accumulates in keratin-containing tissues and is used to treat dermatophyte infections (eg, *Microsporum, Epidermophyton, Trichophyton*).

Educational objective:

The main groups of antifungal drugs are polyenes, azoles, echinocandins, and pyrimidines. Polyene

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~~cell wall. It is active against *Candida* and *Aspergillus*. Caspofungin does not bind ergosterol.~~

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(Choice D) Griseofulvin interacts with fungal cell microtubules, inhibiting mitosis. It accumulates in keratin-containing tissues and is used to treat dermatophyte infections (eg, *Microsporum, Epidermophyton, Trichophyton*).

Educational objective:
The main groups of antifungal drugs are polyenes, azoles, echinocandins, and pyrimidines. Polyene antifungals (eg, amphotericin B, nystatin) act by binding ergosterol in the fungal cell membrane.

Microbiology	Infectious Diseases	Antibiotic resistance
Subject	System	Topic

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A 30-year-old primigravid woman at 35 weeks gestation comes to the emergency department due to fever, nausea, vomiting, watery diarrhea, and myalgias that began one day ago. She has no contractions, vaginal bleeding, or leakage of fluid. Temperature is 39.3 C (102.7 F), blood pressure is 90/60 mm Hg, and pulse is 126/min. The abdomen is soft, and the uterus is nontender. Fetal heart rate is 180/min on Doppler ultrasound. The remainder of the physical examination is normal. Blood cultures grow gram-positive rods. Which of the following is the major virulence factor of the organism responsible for this patient's clinical presentation?

A. Cytotoxin that creates pores in phagosomes
B. Endotoxin-mediated complement and tissue factor activation
C. Exotoxin inhibition of neurotransmitter release
D. Exotoxin-mediated inhibition of elongation factor

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- A. Cytotoxin that creates pores in phagosomes (44%)
- B. Endotoxin-mediated complement and tissue factor activation (30%)
- C. Exotoxin inhibition of neurotransmitter release (7%)
- D. ~~Exotoxin-mediated inhibition of elongation factor~~ (18%)

Correct

44% Answered correctly

02 mins, 15 secs Time Spent

12/18/2020 Last Updated

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Gram-positive rods in blood cultures
• *Corynebacterium* species (diphtheroid) • *Clostridium* species • *Nocardia* species or the anaerobic *Actinomyces* species • *Listeria* species

This pregnant woman has **febrile gastroenteritis** (eg, fever, vomiting, diarrhea) and **gram-positive rods** in her bloodstream, raising strong suspicion for ***Listeria monocytogenes*** infection. *L monocytogenes* is a motile, **facultatively intracellular** organism with several unique adaptations that allow it to evade the host immune response, including the following:

- **Listeriolysin O**: This major virulence factor generates **pores in phagosome** membranes, which allows phagocytosed *L monocytogenes* to **escape into the cytoplasm** of monocytes and avoid lysosomal destruction.
- **Actin-based transcellular spread**: The organism hijacks the actin-based cellular motility mechanism of host cells, which allows it to spread to adjacent cells without reentering the extracellular space. This significantly reduces exposure of *L monocytogenes* to antibodies and phagocytic cells.

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Because of these adaptations, antibody- and phagocyte-mediated destruction of the pathogen is impaired; therefore, infections are controlled primarily by the cytotoxic T-cell response.

Most *L monocytogenes* infections occur in **pregnant women** in the third trimester. Although antibiotics are curative, *L monocytogenes* quickly invades the placenta and may cause fetal death, premature birth, and neonatal infection.

(Choice B) Bacterial lipopolysaccharide (endotoxin) is the major component of the cell wall in gram-negative, not gram-positive, bacteria (some sources erroneously report that *L monocytogenes* contains lipopolysaccharide). Endotoxin activates complement, coagulation, and fibrinolysis, which can lead to septic shock and disseminated intravascular coagulation.

(Choice C) *Clostridium botulinum*, an anaerobic gram-positive rod, produces an exotoxin (botulinum toxin) that inhibits the synaptic transmission of motor neurons. Patients typically develop descending, symmetric motor deficits; minimal sensory changes; and no fever.

(Choice D) Pathogenic strains of *Corynebacterium diphtheriae* produce an exotoxin that inhibits elongation factor in host cells, which causes pseudomembranous pharyngitis and myocarditis. Although *C diphtheriae* is a gram-positive rod, it does not cause febrile gastroenteritis.

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Educational objective:

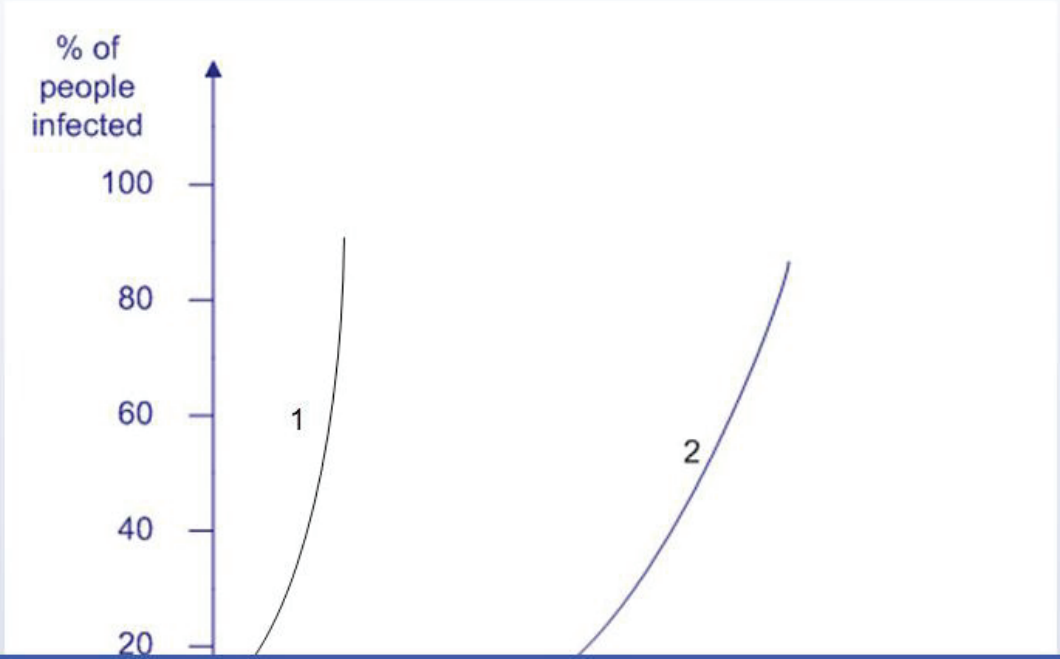
Listeria monocytogenes is a facultative intracellular, gram-positive rod that most often causes febrile gastroenteritis. Pathogenesis is mediated largely by listeriolysin O, an enzyme that creates pores in phagosomes, which allows the bacteria to escape lysosomal destruction. Pregnant women in the third trimester are at greatest risk; infection increases the risk of fetal demise, early labor, and neonatal infection.

Microbiology	Infectious Diseases	Listeria
Subject	System	Topic

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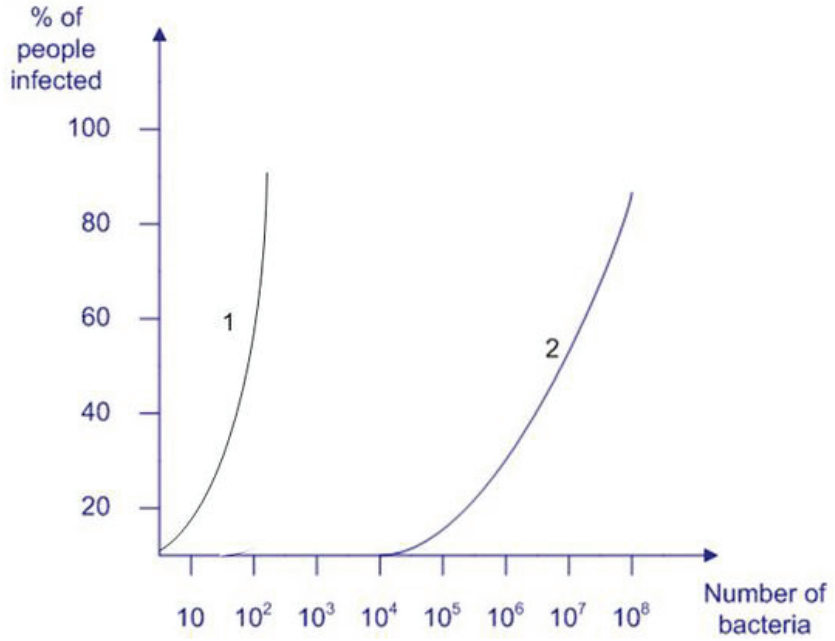
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Volunteer studies are used to determine the infectious dose of *Salmonella* required to cause gastroenteritis. The curve obtained during the studies is shown in the diagram as line 2. Which of the following organisms could be represented by line 1 on this diagram?



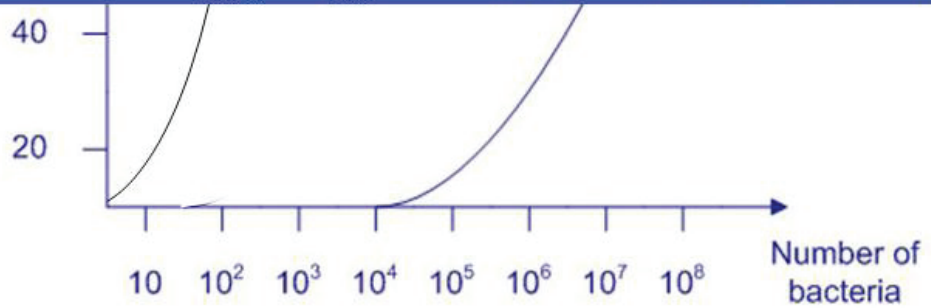
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A. *Clostridium perfringens*

B. Enterotoxigenic *Escherichia coli*

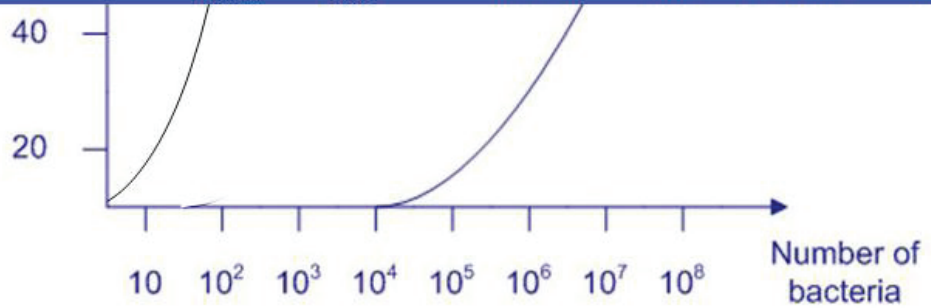
C. *Shigella flexneri*

D. *Vibrio cholerae*

E. *Vibrio parahaemolyticus*

Submit

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A. *Clostridium perfringens* (4%)

B. Enterotoxigenic *Escherichia coli* (9%)

C. *Shigella flexneri* (73%)

D. *Vibrio cholerae* (12%)

E. *Vibrio parahaemolyticus* (0%)

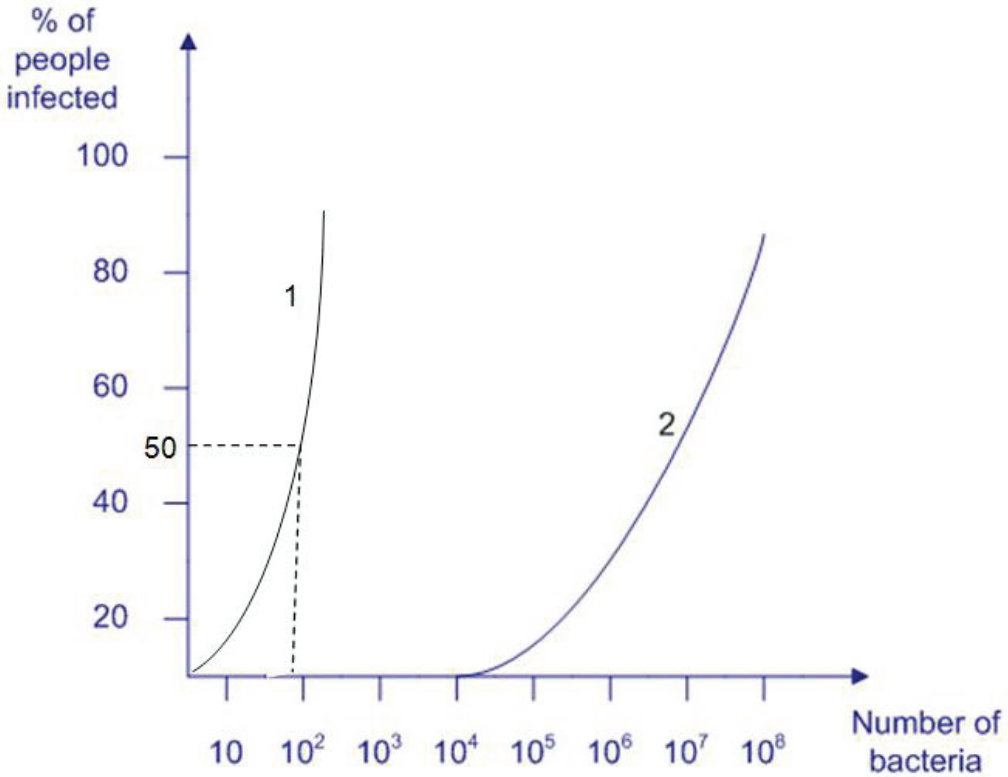
Correct

73%

30 secs

03/26/2021

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The **50% infectious** dose (ID_{50}) corresponds to the minimum number of organisms required to cause disease in 50% of affected individuals. The organism in Line 1 has an ID_{50} ~10^2. Depending on the age and condition of the host and on the species of ***Shigella***, as few as 10 *Shigella* organisms can cause disease. For example, the ID_{50} for *S dysenteriae* is 10, for *S flexneri* is 100, and for *S sonnei* is 500. *Shigella* is able to invade tissues and is highly adapted to surviving the acidity of the stomach and the bacteriostatic action of bile. The incubation period for shigellosis is 24-72 hours. Disease begins with watery diarrhea and progresses to fever, abdominal pain, dysentery, and tenesmus (painful rectal spasm associated with the urge to defecate but little passage of stool). A much larger inoculum of *Salmonella* (approximately 10^7) is required for successful infection in a susceptible host.

Other organisms that can cause diarrhea with only a small inoculum include *Campylobacter jejuni* (around 500 cells), *Entamoeba histolytica* (as few as 1-10 organisms), and *Giardia lamblia* (as few as 1-10 organisms).

(Choices A, B, D, and E) In general, the ID_{50} for *Salmonella*, *Vibrio*, *Clostridium perfringens*, and *Escherichia coli* are high (10^4-10^8).

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(Choices A, B, D, and E) In general, the ID_{50} for *Salmonella*, *Vibrio*, *Clostridium perfringens*, and *Escherichia coli* are high (10^4-10^8).

Educational objective:
Depending on the age and condition of the host and the species of *Shigella*, as few as 10-500 cells can cause infection.

Microbiology	Infectious Diseases	Acute diarrhea
Subject	System	Topic

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A 34-year-old man comes to the office due to disabling fatigue. The patient was diagnosed with paroxysmal nocturnal hemoglobinuria 3 years prior and has required numerous blood transfusions due to anemia. Treatment will be initiated with a monoclonal antibody to the complement component C5. This patient requires immunization and prophylactic pharmacotherapy to prevent infection with which of the following organisms?

A. *Escherichia coli*
B. Herpes zoster virus
C. *Mycobacterium tuberculosis*
D. *Neisseria meningitidis*
E. *Staphylococcus aureus*

Submit

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A 34-year-old man comes to the office due to disabling fatigue. The patient was diagnosed with paroxysmal nocturnal hemoglobinuria 3 years prior and has required numerous blood transfusions due to anemia. Treatment will be initiated with a monoclonal antibody to the complement component C5. This patient requires immunization and prophylactic pharmacotherapy to prevent infection with which of the following organisms?

- A. *Escherichia coli* (1%)
- B. Herpes zoster virus (0%)
- C. *Mycobacterium tuberculosis* (3%) ✗
- D. *Neisseria meningitidis* (92%) ✓
- E. *Staphylococcus aureus* (2%)

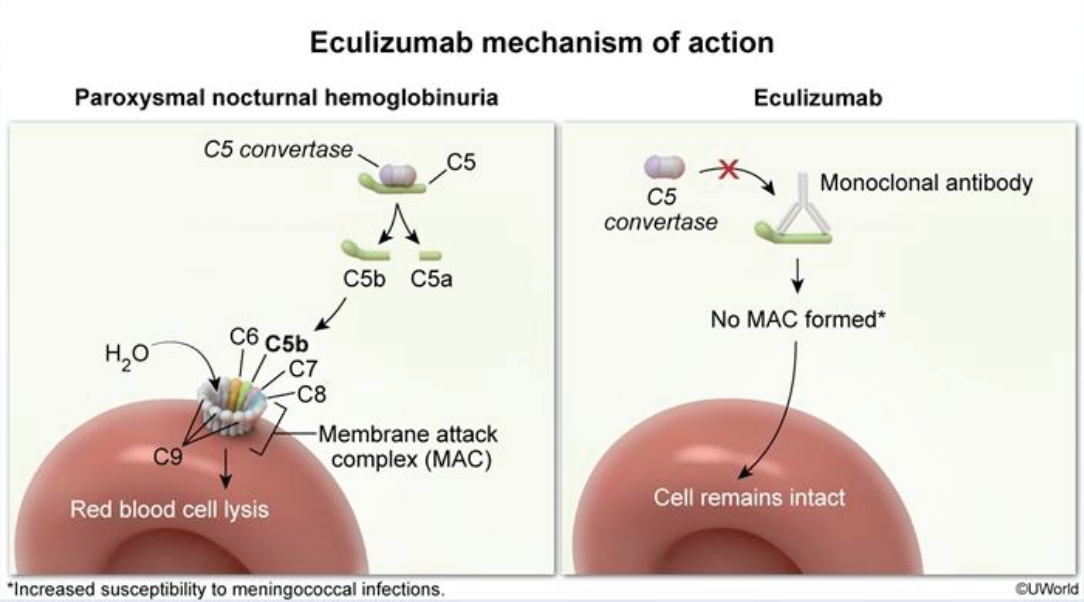
Incorrect
Correct answer
D

92%
Answered correctly

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This patient has **paroxysmal nocturnal hemoglobinuria** (PNH), a condition resulting from decreased expression of complement-inactivating proteins (eg, CD55, CD59) on the surface of red blood cells. This leads to increased formation of the membrane attack complex (MAC) (eg, complement components C5b-C9), resulting in anemia due to **complement-mediated hemolysis**. Patients with debilitating PNH

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*Increased susceptibility to meningococcal infections.

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This patient has **paroxysmal nocturnal hemoglobinuria** (PNH), a condition resulting from decreased expression of complement-inactivating proteins (eg, CD55, CD59) on the surface of red blood cells. This leads to increased formation of the membrane attack complex (MAC) (eg, complement components C5b-C9), resulting in anemia due to **complement-mediated hemolysis**. Patients with debilitating PNH symptoms (eg, fatigue, thrombosis, transfusion requirement) are often **treated with a monoclonal antibody** (eg, eculizumab) to a terminal complement component (ie, C5), which **inhibits the formation of MAC** and decreases the severity of PNH symptoms.

However, inhibition of terminal complement activity and MAC formation also results in **loss of the rapid complement-mediated killing** of Gram-negative bacteria, especially ***Neisseria meningitidis***, which can proliferate and disseminate quickly to cause catastrophic systemic disease. Therefore, patients receiving anti-complement therapy should be immunized against *N meningitidis* and be given appropriate antibiotic prophylaxis (eg, penicillin).

(Choices A and E) Most strains of *Escherichia coli* and *Staphylococcus aureus* produce factors that evade complement or inhibit complement activation and do not replicate as rapidly as *N meningitidis*. Therefore, host defense to these pathogens depends primarily on other components of the immune system

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prophylaxis (eg, penicillin).

(Choices A and E) Most strains of *Escherichia coli* and *Staphylococcus aureus* produce factors that evade complement or inhibit complement activation and do not replicate as rapidly as *N meningitidis*. Therefore, host defense to these pathogens depends primarily on other components of the immune system (eg, neutrophil function, humoral immunity) and would not be significantly affected by the use of a terminal complement inhibitor.

(Choices B and C) Host defense to herpes zoster virus and *Mycobacterium tuberculosis* depends more on T cell function than complement activation and MAC formation.

Educational objective:
Paroxysmal nocturnal hemoglobinuria may be treated with a monoclonal antibody to the complement component C5 (ie, terminal complement inhibitor), increasing the risk of disseminated *Neisseria meningitidis* infection. Therefore, these patients should receive immunization and antibiotic prophylaxis against *N meningitidis*.

References

- Eculizumab: a review of its use in paroxysmal nocturnal haemoglobinuria.

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A 31-year-old man comes to the office due to oral lesions that cause occasional discomfort during eating. He also reports fatigue and unintentional weight loss. The patient has no prior medical problems and takes no medications. Oral examination findings are shown below.



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The lesions can be easily scraped off, revealing erythematous mucosa underneath. There are several enlarged cervical and axillary lymph nodes. Which of the following diagnostic tests is most appropriate during further workup of this patient?

A. HIV antigen and antibody testing

B. Oral lesion biopsy to rule out malignancy

C. PCR for coxsackievirus

D. Scraping microscopy for multinucleated giant cells

E. Serum vitamin B_{12} and folate levels

Submit

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The lesions can be easily scraped off, revealing erythematous mucosa underneath. There are several enlarged cervical and axillary lymph nodes. Which of the following diagnostic tests is most appropriate during further workup of this patient?

- A. HIV antigen and antibody testing (88%)
- B. Oral lesion biopsy to rule out malignancy (7%)
- C. PCR for coxsackievirus (0%)
- D. Scraping microscopy for multinucleated giant cells (3%)
- E. Serum vitamin B_{12} and folate levels (0%)

Correct

88%
Answered correctly

52 secs
Time Spent

12/07/2020
Last Updated

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Thrush is an oropharyngeal ***Candida albicans* infection** that usually presents with creamy white, plaque-like lesions on the buccal mucosa, palate, tongue, or pharynx. The lesions can be **easily scraped off** with a tongue depressor, revealing underlying erythematous mucosa. The diagnosis is often made clinically, but microscopic examination will reveal budding yeasts with or without pseudohyphae.

Candida albicans is a normal commensal of the human digestive tract that can cause mucocutaneous infections when local microbial flora is disrupted (eg, antibiotic use) or the cell-mediated immune response is impaired. Although *Candida* infections of the skin (eg, diaper rash) and vulvovaginal region often occur in otherwise healthy individuals, oropharyngeal infection is rare in the absence of antibiotics, chemotherapy, or inhaled corticosteroids. Young, healthy individuals who develop thrush and have no clear inciting cause should be tested for **HIV**, particularly when HIV risk factors (eg, multiple sexual partners) or symptoms of the virus (eg, **lymphadenopathy**, **weight loss**) are present. A fourth-generation **HIV antigen/antibody test** is typically used for screening.

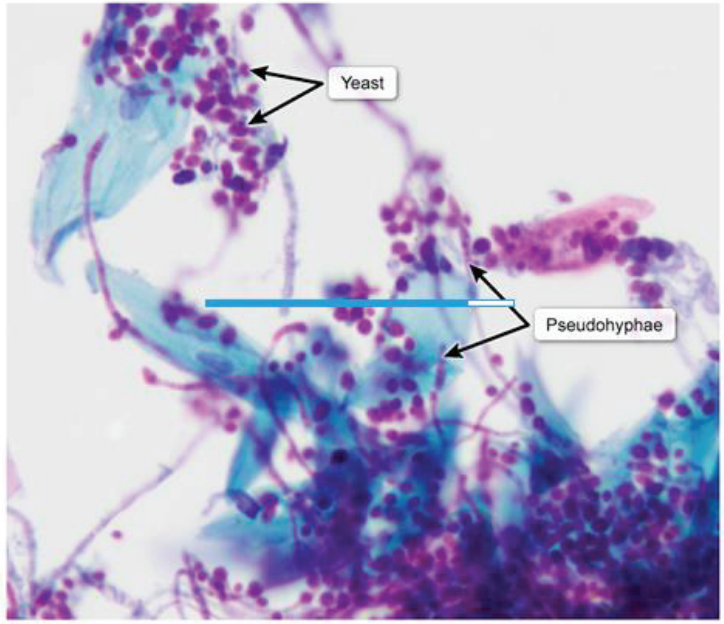
(Choice B) Leukoplakia is a benign lesion of the tongue caused by hyperplasia of the squamous mucosa that can evolve into dysplasia → carcinoma in situ → invasive carcinoma. Leukoplakia appears as white patches or plaques on the oral mucosa. However, these lesions cannot be easily removed with scraping (unlike thrush).

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Candida albicans

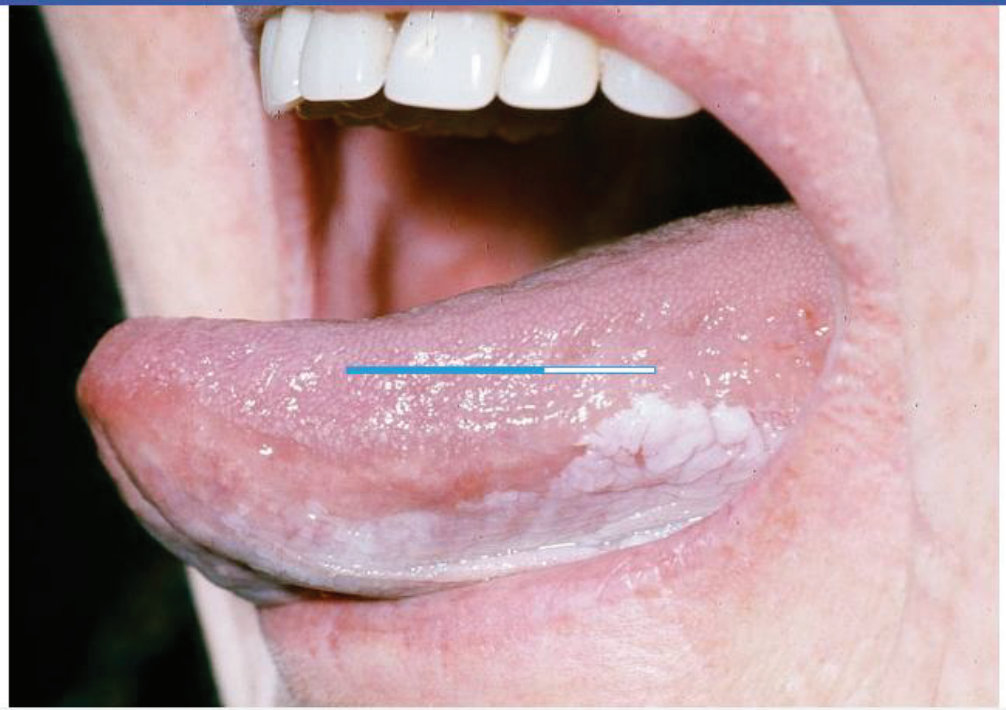


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(unlike thrush).

(Choice C) Coxsackievirus causes herpangina, which is usually seen in infants and children. It is characterized by high fever, sore throat, and yellowish or grey-white papulovesicular lesions on the throat (tongue lesions are rare). Coxsackievirus also causes hand, foot, and mouth disease, which is characterized by tongue macules, vesicles, and ulcers. However, it is also usually associated with a vesicular or macular skin rash.

(Choice D) Microscopy of herpes simplex virus (HSV) lesions will reveal multinucleated giant cells. HSV usually causes multiple vesicular lesions on an erythematous base, not white mucosal plaques.

(Choice E) Atrophic glossitis can be caused by vitamin B_{12} or folate deficiency. It is characterized by atrophy of the filiform papillae leading to a smooth, glossy, erythematous tongue.

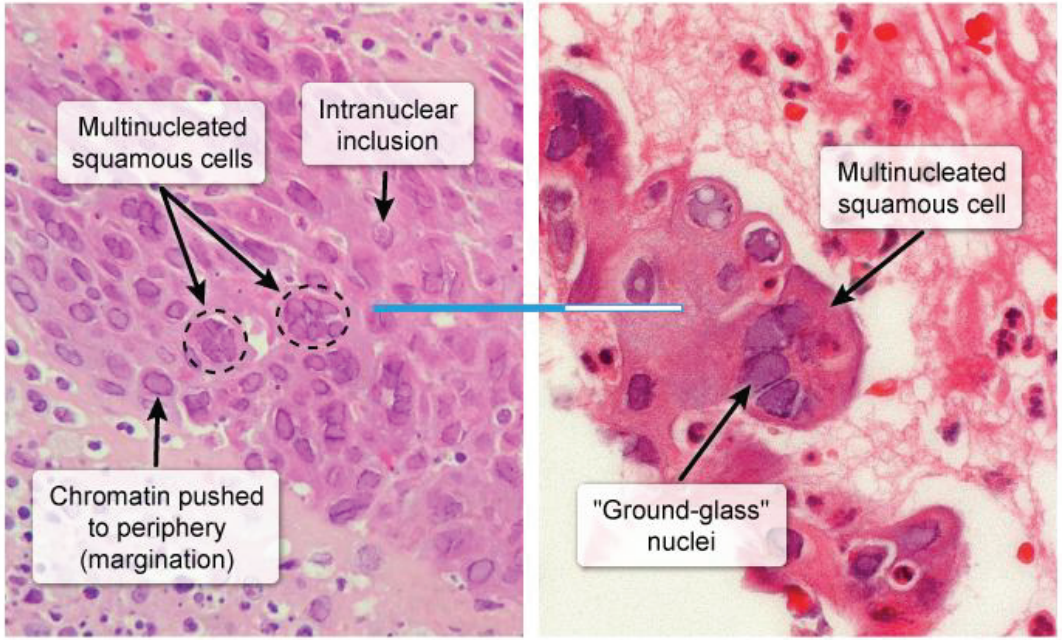
Educational objective:
Oral thrush is caused by *Candida albicans* infection and usually presents as white, plaque-like oropharyngeal lesions that are easily scraped off with a tongue depressor. Affected patients typically have disruption to local microbial flora (eg, antibiotic use) or impairment in cell-mediated immunity (eg, corticosteroids, HIV). Young, otherwise healthy patients with thrush should be tested for HIV, particularly if they have HIV risk factors or other symptoms of the virus.

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(unlike thrush).

Exhibit Display

Herpes simplex virus



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A 21-year-old man comes to the office due to several days of intense pruritus of the inguinal-genital area. He has had no fever, dysuria, or skin rash. He is not using any new soaps, detergents, or lotions. The patient has had 3 sexual partners in the past year. He was treated for chlamydial urethritis 6 months ago and since then has been using condoms consistently. Vital signs are within normal limits. Genitourinary examination shows no urethral discharge, penile lesions, or inguinal lymphadenopathy. There are skin excoriation marks in the pubic area and other findings as shown in the exhibit. Which of the following is the most appropriate pharmacotherapy for this patient's condition?

A. Oral acyclovir
B. Oral doxycycline
C. Oral fluconazole
D. Topical imiquimod
E. Topical permethrin
F. Topical triamcinolone

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He has had no fever, dysuria, or skin rash. He is not using any new soaps, detergents, or lotions. The patient has had 3 sexual partners in the past year. He was treated for chlamydial urethritis 6 months ago and since then has been using condoms consistently. Vital signs are within normal limits. Genitourinary examination shows no urethral discharge, penile lesions, or inguinal lymphadenopathy. There are skin excoriation marks in the pubic area and other findings as shown in the exhibit. Which of the following is the most appropriate pharmacotherapy for this patient's condition?

A. ~~Oral acyclovir~~ (3%)
B. ~~Oral doxycycline~~ (7%)
C. ~~Oral fluconazole~~ (10%)
D. Topical imiquimod (7%)
E. Topical permethrin (63%)
F. ~~Topical triamcinolone~~ (6%)

Correct

63%
38 secs
10/21/2020

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Phthirus pubis, the human pubic louse, is a translucent parasite approximately 1 mm long with crab-like claws that allow it to grip pubic hair. Transmission usually occurs during **sexual contact** whereby an infected individual transmits the louse to an uninfected individual by skin-to-skin contact. Therefore, condoms are unable to prevent transmission (it is not transmitted by fluids). Teenagers and **young adults** are affected most commonly due to higher numbers of sexual partners.

Manifestations typically include **intense pruritus** in the pubic area with excoriations due to scratching. Other hairy areas such as the axillae may be affected, but the scalp is typically spared. Visualization of the louse or nits (oval, white, louse eggs on the hair shaft) confirms the diagnosis. First-line treatment includes a **topical permethrin cream** to the affected area. Permethrin blocks parasite sodium ion conduction in nerve cell membrane channels and results in louse paralysis and death.

(Choice A) Oral acyclovir is used for genital herpes simplex virus infection, which usually causes painful vesicular genital lesions on an erythematous base.

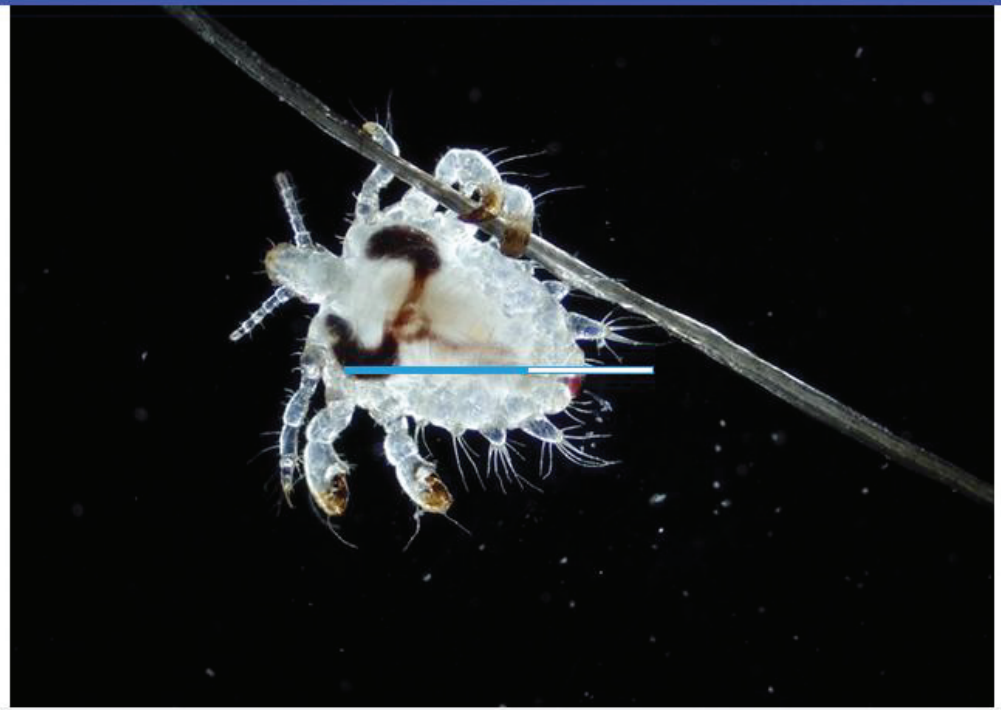
(Choice B) Oral doxycycline is first-line treatment for hidradenitis suppurativa, a chronic follicular occlusive disease that manifests in the intertriginous skin areas (eg, groin, axilla, inframammary). Manifestations usually include recurrent inflammatory nodules and abscesses with pain and malodorous discharge.

(Choice C) Oral fluconazole can be used to treat mucocutaneous *Candida* infections. *Candida* balanitis

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(Choice C) Oral fluconazole can be used to treat mucocutaneous *Candida* infections *Candida* balanitis

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disease that manifests in the intertriginous skin areas (eg, groin, axilla, inframammary). Manifestations usually include recurrent inflammatory nodules and abscesses with pain and malodorous discharge.

(Choice C) Oral fluconazole can be used to treat mucocutaneous *Candida* infections. *Candida* balanitis can cause severe pruritus but would be associated with white patches on an erythematous base.

(Choice D) Topical imiquimod increases the immune-response to anogenital warts due to human papilloma virus infection. It stimulates interferon-alpha, tumor necrosis factor, and interleukin-1/6/8. Anogenital warts can have many presentations (eg, flat, dome-shaped, filiform, pedunculated, verrucous) and may occasionally be pruritic.

(Choice F) Topical corticosteroids can be used to treat inflammatory cutaneous conditions such as psoriasis and contact dermatitis. Although these conditions can cause erythema and pruritus, they would not be associated with a translucent louse on examination.

Educational objective:

Phthirus pubis is the human pubic louse. It is transmitted sexually via skin-to-skin contact and causes intense pruritus. Louse and nits can often be visualized on examination, which is diagnostic. Treatment with topical permethrin is generally curative.

References

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A 35-year-old man is admitted to the hospital after he fell off a moving tractor and caught his right leg underneath the vehicle. The patient has no past medical history. Over the next few hours, he develops worsening severe pain and rapidly increasing swelling in the injured right leg. Crepitus is present on physical examination. Emergent radiographic imaging reveals gas in the tissues. Surgical evaluation is performed. The microorganism most likely responsible for this patient's condition is also commonly associated with which of the following conditions?

A. Heart murmur and valve abscess

B. Persistent cough and pharyngeal exudates

C. Relentless headaches and nausea

D. Transient watery diarrhea and abdominal discomfort

E. Urinary frequency and burning

Submit

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A 35-year-old man is admitted to the hospital after he fell off a moving tractor and caught his right leg underneath the vehicle. The patient has no past medical history. Over the next few hours, he develops worsening severe pain and rapidly increasing swelling in the injured right leg. Crepitus is present on physical examination. Emergent radiographic imaging reveals gas in the tissues. Surgical evaluation is performed. The microorganism most likely responsible for this patient's condition is also commonly associated with which of the following conditions?

A. Heart murmur and valve abscess (12%)
B. Persistent cough and pharyngeal exudates (8%)
C. Relentless headaches and nausea (5%)
✓ D. Transient watery diarrhea and abdominal discomfort (71%)
E. Urinary frequency and burning (2%)

Correct

71% Answered correctly
47 secs Time Spent
10/26/2020 Last Updated

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Spores of ***Clostridium perfringens***, a gram-positive bacillus responsible for ~95% of cases of **gas gangrene** (clostridial myonecrosis), are abundant in soil and can inoculate **penetrating injury** sites. On entering the host, the spores germinate in the **anaerobic** environment into vegetative cells, which produce a phospholipase **toxin** that attacks cell membranes. Extensive tissue damage, **necrosis**, and reduced blood supply to the affected area result, with the disease spreading in the enlarging anaerobic environment. The organism rapidly metabolizes carbohydrates, producing **gas** that can sometimes be felt on examination (crepitus) and may often be **visualized** on radiographs (helping to distinguish gas gangrene from other necrotizing infections). Treatment involves antibiotics and emergent debridement. However, prognosis is poor even with prompt therapy, and tissue loss is often considerable.

C perfringens can also cause late-onset **food poisoning** that is characterized by transient watery diarrhea. This gastroenteritis is caused by a toxin formed when large quantities of clostridial spores are ingested. The spores germinate in the digestive tract and then begin to elaborate toxin, which explains the disease's delayed onset. This is in contrast to early-onset food poisoning caused by the preformed toxins of *Staphylococcus aureus* and *Bacillus cereus*.

(Choices A and B) *C perfringens* does not cause cough. It is also an extremely rare cause of endocarditis and valve abscess.

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Staphylococcus aureus and *Bacillus cereus*.

(Choices A and B) *C perfringens* does not cause cough. It is also an extremely rare cause of endocarditis and valve abscess.

(Choice C) Relentless headaches and nausea can be caused by any organism that causes meningitis. Subacute or chronic infections causing these illnesses include *Mycobacterium tuberculosis, Acanthamoeba*, and *Cryptococcus neoformans*.

(Choice E) Urinary frequency and burning are caused by urethritis/cystitis. The urethritis of urinary tract infections is usually due to *Escherichia coli*, whereas sexually transmitted types of urethritis can be due to gonorrhea, chlamydia, and *Ureaplasma urealyticum*. *C perfringens* does not cause dysuria.

Educational objective:
Clostridium perfringens causes late-onset food poisoning and clostridial myonecrosis (gas gangrene). The food poisoning is toxin-mediated, late-onset, and causes transient watery diarrhea.

Microbiology	Infectious Diseases	Clostridial myonecrosis
Subject	System	Topic

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A 9-month-old girl is brought to the emergency department after a 2-minute generalized seizure. The patient has had a fever for the past 12 hours and has been very fussy. She takes no medications and has no allergies. Her temperature is 39.4 C (103 F). Examination shows no abnormalities, and the patient is discharged home. Three days later, she is afebrile but develops a maculopapular rash on her trunk. Infection with which of the following is the most likely cause of this patient's condition?

A. Coxsackievirus A16
B. Herpes simplex virus type 1
C. *Human herpesvirus 6*
D. Measles virus
E. Parvovirus B19
F. Rubella virus
G. *Streptococcus pyogenes*

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A 9-month-old girl is brought to the emergency department after a 2-minute generalized seizure. The patient has had a fever for the past 12 hours and has been very fussy. She takes no medications and has no allergies. Her temperature is 39.4 C (103 F). Examination shows no abnormalities, and the patient is discharged home. Three days later, she is afebrile but develops a maculopapular rash on her trunk. Infection with which of the following is the most likely cause of this patient's condition?

A. Coxsackievirus A16 (4%)
B. Herpes simplex virus type 1 (2%)
C. *Human herpesvirus 6* (50%)
D. Measles virus (19%)
E. Parvovirus B19 (5%)
F. Rubella virus (14%)
G. *Streptococcus pyogenes* (3%)

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Roseola infantum	
Microbiology	• HHV-6 most common
Epidemiology	• Age <2 years
Clinical features	• 3-5 days of high fever followed by blanching maculopapular rash
Treatment	• Supportive care

HHV-6 = human herpesvirus 6.

This patient's presentation is consistent with **roseola infantum**, which is most commonly caused by ***human herpesvirus 6* (HHV-6)**. Febrile seizures can be caused by any febrile illness, and HHV-6 is one of the most common causes. However, most patients with HHV-6 infection do not develop seizures. Primary symptoms include **high fever** for 3-5 days **followed by an erythematous maculopapular rash**. The rash usually **starts on the trunk** and spreads to the face and extremities. The diagnosis is based on clinical presentation, and the infection is typically benign and self-limited.

(Choice A) Coxsackievirus A16 is a common cause of hand-foot-mouth disease in children. Patients typically have erythematous oropharyngeal ulcers and maculopapular or vesicular lesions on the palms and

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presentation, and the infection is typically benign and self-limited.

(Choice A) Coxsackievirus A16 is a common cause of hand-foot-mouth disease in children. Patients typically have erythematous oropharyngeal ulcers and maculopapular or vesicular lesions on the palms and soles.

(Choice B) Children with primary infection with herpes-simplex virus type 1 (HSV-1) have painful gingivostomatitis, often accompanied by fever and irritability. Neonatal HSV, most commonly caused by HSV-2, can present with fever and seizures in the newborn period.

(Choices D and F) Rubella and measles are vaccine-preventable viral infections that typically present with a maculopapular rash on the face that then spreads to the trunk and extremities. Both infections can be distinguished from roseola by the pattern of rash development. In addition, patients with rubella often have Forchheimer spots on the soft palate, and measles is characterized by pathognomonic Koplik spots on buccal mucosa.

(**Choice E**) Parvovirus B19 causes erythema infectiosum, or fifth disease, which can present as a flulike illness followed by a characteristic "slapped cheek" rash and truncal reticular rash. Parvovirus B19 can be associated with an aplastic crisis in those with pre-existing hematologic abnormalities (eg, sickle cell anemia).

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presentation, and the infection is typically benign and self-limited.

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presentation, and the infection is typically benign and self-limited.

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illness followed by a characteristic "slapped cheek" rash and truncal reticular rash. Parvovirus B19 can be associated with an aplastic crisis in those with pre-existing hematologic abnormalities (eg, sickle cell anemia).

(Choice G) *Streptococcus pyogenes* (Group A *Streptococcus*) can cause acute, exudative pharyngitis that is associated with fever, headache, and abdominal pain in school-aged children. It can also be accompanied by scarlet fever, a diffuse "sandpaper"-textured rash most prominent in skinfolds (eg, groin, axillae, antecubital fossa).

Educational objective:

Human herpesvirus 6 infection (roseola) classically presents with fever for 3-5 days followed by a truncal rash. It is also the most common cause of febrile seizures.

References

- Roseola infantum and its causal human herpesviruses.

Microbiology	Infectious Diseases	Human herpesvirus 6
Subject	System	Topic

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A 28-year-old woman comes to the office due to several months of progressive abdominal pain and intermittent diarrhea. She denies fever or chills but has lost weight due to poor appetite. The patient works for an organization that installs wood pellet cookstoves in rural villages in Central Africa and has spent much time in the region over the last 5 years. Temperature is 37.8 C (100 F), blood pressure is 126/72, and pulse is 86. BMI is 19 kg/m^2. Physical examination is normal. Laboratory results are as follows:

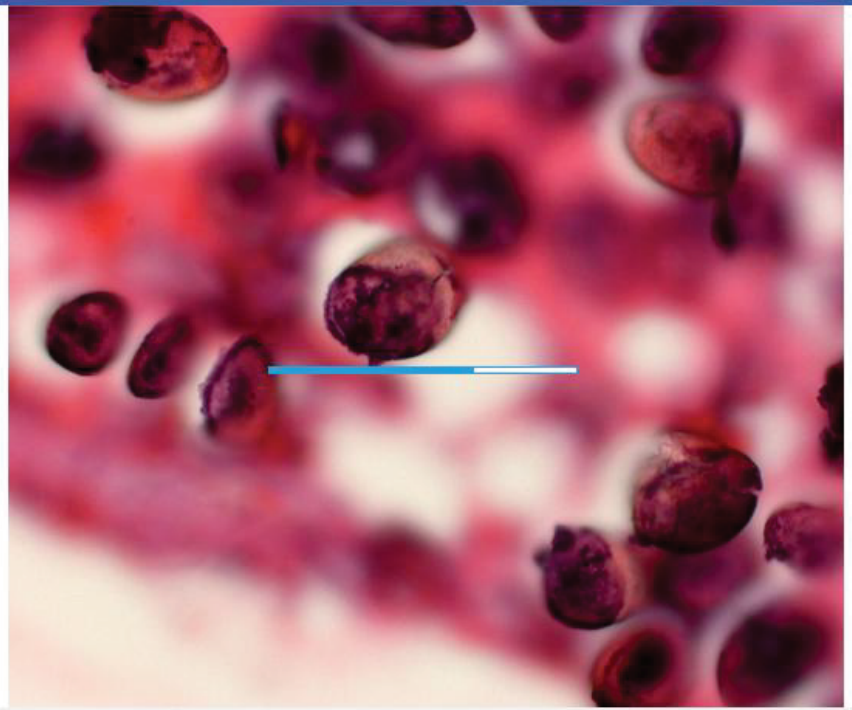
Complete blood count	
Hemoglobin	9.5 g/dL
Platelets	195,000/mm^3
Leukocytes	8,800/mm^3
Neutrophils	54%
Eosinophils	14%
Lymphocytes	32%

An intestinal biopsy sample is shown in the exhibit. Which of the following is the most appropriate treatment for this patient?

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treatment for this patient?

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Leukocytes	8,800/mm^3
Neutrophils	54%
Eosinophils	14%
Lymphocytes	32%

An intestinal biopsy sample is shown in the exhibit. Which of the following is the most appropriate treatment for this patient?

A. Artemisinin-based combination therapy
B. Ciprofloxacin
C. Ganciclovir
D. Metronidazole plus paromomycin
E. Praziquantel

Submit

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Leukocytes	8,800/mm^3
Neutrophils	54%
Eosinophils	14%
Lymphocytes	32%

An intestinal biopsy sample is shown in the exhibit. Which of the following is the most appropriate treatment for this patient?

A. Artemisinin-based combination therapy (7%)
B. Ciprofloxacin (1%)
C. Ganciclovir (0%)
D. Metronidazole plus paromomycin (38%)
E. Praziquantel (52%)

Correct
52%
41 secs
01/06/2021

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Schistosomiasis		
***Schistosoma* species**	**Location**	**Symptoms**
S haematobium	• North Africa • Sub-Saharan Africa • Middle East	**Urinary schistosomiasis** • Terminal hematuria, dysuria & frequent urination • Hydronephrosis, pyelonephritis & squamous cell carcinoma of the bladder
S mansoni	• Sub-Saharan Africa • Middle East • South America • Caribbean	**Intestinal schistosomiasis** • Diarrhea & abdominal pain • Intestinal ulceration → iron deficiency anemia **Hepatic schistosomiasis** • Hepatomegaly, splenomegaly • Periportal fibrosis & subsequent portal hypertension
S japonicum	• Asia, particularly China • Philippines	

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S japonicum	• Asia, particularly China • Philippines • Japan	• Hepatomegaly, splenomegaly • Periportal fibrosis & subsequent portal hypertension

This patient's travel history, chronic intestinal symptoms, eosinophilia, and biopsy findings suggest **schistosomiasis**, a parasitic blood fluke infection primarily seen in rural parts of **sub-Saharan Africa** and East Asia. Exposure occurs when humans swim or bathe in freshwater that contains **contaminated snails** (the intermediate host). Cercariae from the snails penetrate human skin and migrate to the **liver**, where they mature into adult worms. Adult worms then travel through the portal circulation to the **mesenteric** venules (*S mansoni* and *S japonicum*) or the venous plexus of the **bladder** (*S haematobium*).

Adult worms release eggs through host tissue to be excreted in feces or urine. Although most patients are asymptomatic, eggs can trigger a significant **granulomatous inflammatory response**, leading to manifestations in the **gastrointestinal tract** (eg, diarrhea, weight loss, anorexia, anemia), bladder (eg, terminal hematuria), or periportal system (eg, portal hypertension, splenomegaly). **Eosinophilia** is common early in the disease course as eosinophils release granules that are toxic to adult worms.

Diagnostic confirmation requires the identification of **round/oval eggs** with a characteristic terminal (*S.*

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terminal hematuria), or periportal system (eg, portal hypertension, splenomegaly). **Eosinophilia** is common early in the disease course as eosinophils release granules that are toxic to adult worms.

Diagnostic confirmation requires the identification of **round/oval eggs** with a characteristic terminal (*S. haematobium*) or lateral (*S. mansoni*) spine on stool/urinary testing or tissue biopsy. Treatment with **praziquantel**, which alters parasite digestion and calcium transport, is generally curative.

(Choice A) Artemisinin-based combination therapy is used for chloroquine resistant malaria. Malaria can cause gastrointestinal symptoms, but patients are usually acutely ill (eg, fever, chills, myalgia, headache). Giemsa-stained blood smear generally reveals intraerythrocytic ring-shaped trophozoites, not eggs with a spine.

(Choice B) Bacterial infection of the gastrointestinal tract is common when traveling to countries with poor sanitation and water control systems. Ciprofloxacin is sometimes used for treatment. However, most cases are brief in duration, eosinophilia is not generally seen, and eggs would not be present.

(Choice C) Ganciclovir can treat cytomegalovirus colitis, which frequently causes diarrhea and abdominal pain. However, most cases arise in patients that are severely immunocompromised. Furthermore, fever is usually present and biopsy would show intracytoplasmic and intranuclear inclusions, not eggs.

(Choice D) Metronidazole plus paromomycin is used to treat *Entamoeba histolytica*, which is a common

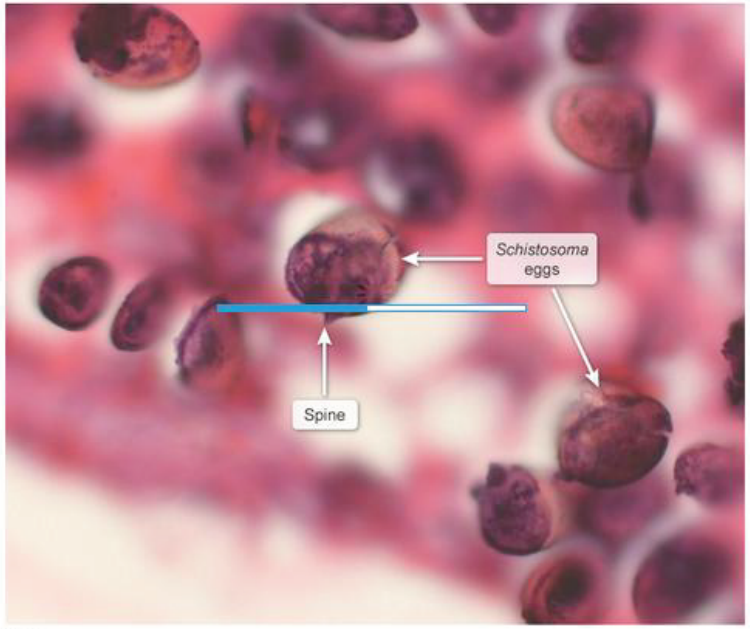
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terminal hematuria), or periportal system (eg, portal hypertension, splenomegaly). **Eosinophilia** is

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Schistosomiasis



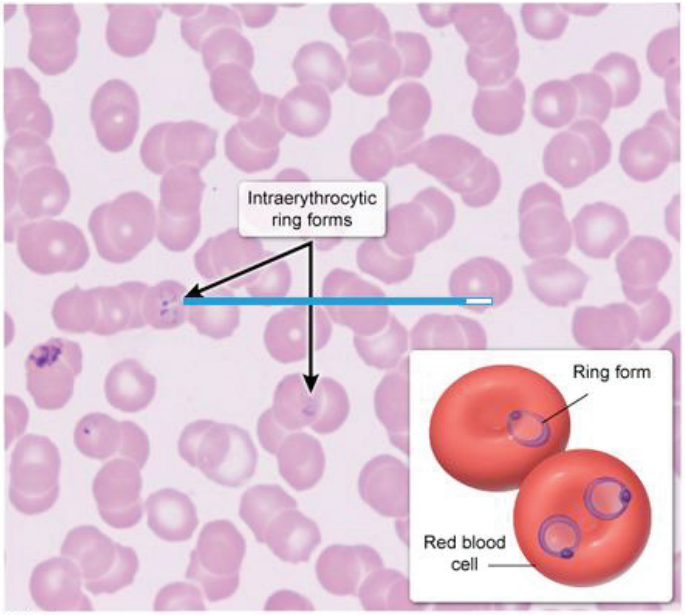
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terminal hematuria), or periportal system (eg, portal hypertension, splenomegaly). **Eosinophilia** is

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Plasmodium falciparum



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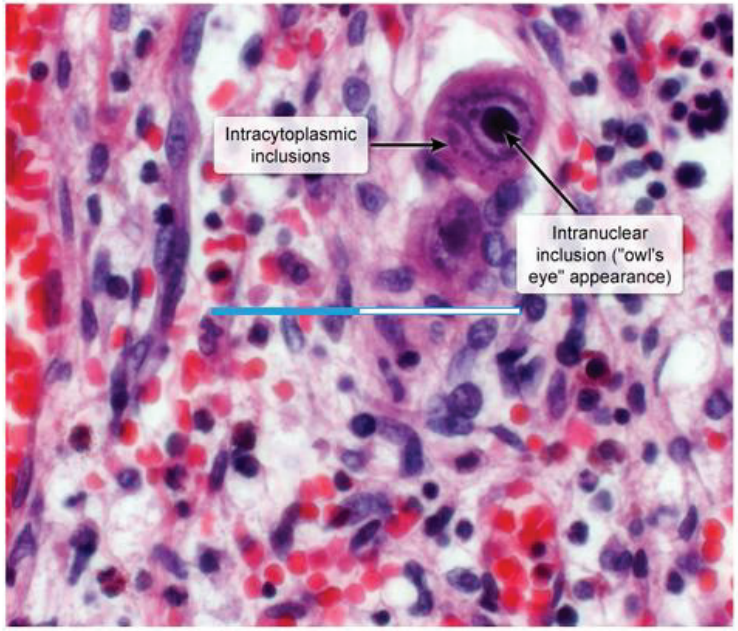
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terminal hematuria), or periportal system (eg, portal hypertension, splenomegaly). **Eosinophilia** is

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Cytomegalovirus



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sanitation and water control systems. Ciprofloxacin is sometimes used for treatment. However, most cases are brief in duration, eosinophilia is not generally seen, and eggs would not be present.

(Choice C) Ganciclovir can treat cytomegalovirus colitis, which frequently causes diarrhea and abdominal pain. However, most cases arise in patients that are severely immunocompromised. Furthermore, fever is usually present and biopsy would show intracytoplasmic and intranuclear inclusions, not eggs.

(Choice D) Metronidazole plus paromomycin is used to treat *Entamoeba histolytica*, which is a common cause of dysentery (eg, diarrhea, fever, abdominal pain) in travelers. However, the presence of several months of symptoms, eosinophilia, and eggs on biopsy make this diagnosis unlikely.

Educational objective:
Schistosomiasis is a blood fluke infection that occurs when humans bathe or swim in freshwater that contains contaminated snails. Adult worms mature in the liver, lodge in the mesenteric venules or vesicular venous plexus, and secrete eggs into feces or urine. Eggs can trigger granulomatous inflammation, leading to symptoms in the gastrointestinal, urinary, or periportal tract. Diagnosis is typically made when round or oval eggs with a terminal or lateral spine are identified in urine, feces, or biopsy.

Pharmacology Infectious Diseases Schistosomiasis

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A 43-year-old man comes to the office due to increasing discomfort and pain with sitting for the past several months. He also has had occasional perianal pruritus. Physical examination shows multiple, cauliflower-shaped, verrucous growths measuring 1 to 2 cm on the perianal skin. Histopathologic examination of one of the lesion reveals hyperplastic papillary squamous epithelium with parakeratosis, nuclear irregularity, and "perinuclear halos" of cytoplasmic vacuolization. Which of the following additional studies is most appropriate for this patient at this time?

A. Adhesive paddle test with microscopy
B. Colonoscopy with terminal ileoscopy
C. Darkfield microscopy of the tissue
D. Hepatic venous pressure measurement
E. HIV antigen and antibody testing

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A. Adhesive paddle test with microscopy (6%)
B. Colonoscopy with terminal ileoscopy (12%)
C. Darkfield microscopy of the tissue (11%)
D. Hepatic venous pressure measurement (1%)
✓ E. HIV antigen and antibody testing (68%)

Correct

68%
Answered correctly

01 min, 55 secs
Time Spent

11/11/2020
Last Updated

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Condylomata acuminata (anogenital warts)	
Etiology	• Human papillomavirus types 6 & 11 • May have coinfection with other genotypes
Appearance	• Plaques, papules, verrucous lesions • Genitalia, perineum, perianal skin
Biopsy	• Thickening of the stratum corneum • Epidermal hyperplasia • Cytoplasmic vacuolization
Disease associations & risk factors	• HIV • Other sexually transmitted infections • Immune suppression

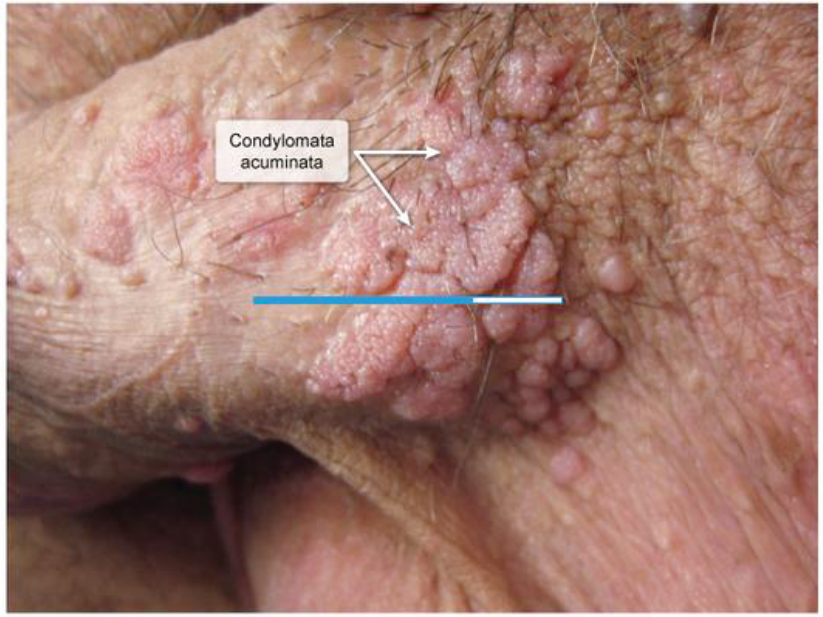
Condylomata acuminata (anogenital warts [AGW]) are characterized by pink or skin-colored plaques, papules, and verrucous lesions on the genitalia, perineum, or perianal skin. AGW are caused by **human papillomavirus** (HPV), primarily **types 6 and 11**. The diagnosis is usually apparent on clinical examination, but biopsy is often helpful for large or atypical lesions. Histopathologic features include

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Condylomata acuminata



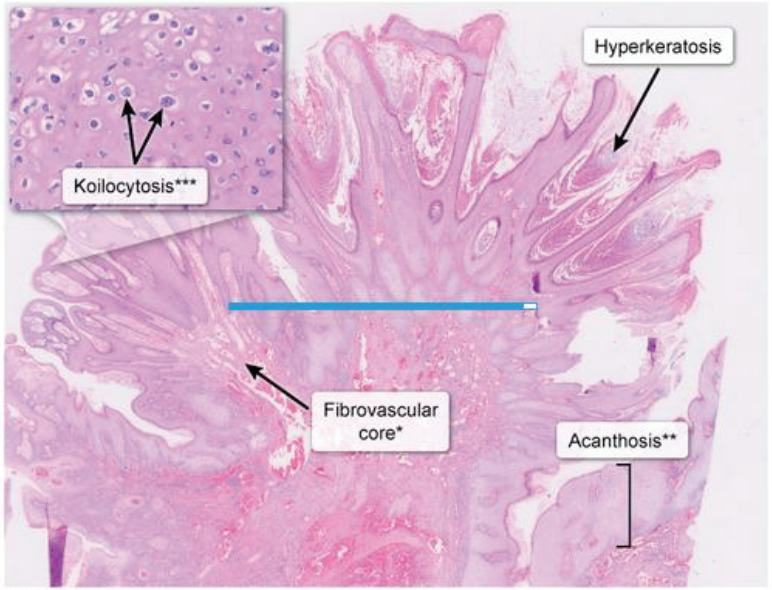
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examination, but biopsy is often helpful for large or atypical lesions. Histopathologic features include

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Condyloma acuminatum



*Papillary architecture shows fibrovascular cores lined by epithelial cells
**Thickened epidermis
***Irregular nuclei with perinuclear halos

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examination, but biopsy is often helpful for large or atypical lesions. Histopathologic features include

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examination, but biopsy is often helpful for large or atypical lesions. Histopathologic features include **papillary architecture** with thickening of the stratum corneum (hyperkeratosis), epidermal hyperplasia (acanthosis), nuclear irregularity, and **perinuclear vacuolization** (koilocytosis).

AGW are associated with an increased **risk for HIV infection**. AGW and HIV share common risk factors; both are frequently acquired via sexual contact and have an increased prevalence in men who have sex with men. In addition, patients with immune suppression (eg, transplant immunosuppression, HIV infection) have increased incidence of AGW and frequently have multiple, widespread lesions. Conversely, large, friable AGW lesions likely confer increased susceptibility to acquiring HIV infection. Therefore, **HIV testing** is recommended.

(Choice A) Pinworm (*Enterobius vermicularis*) infection is confirmed on microscopy after sampling the perianal area for eggs with an adhesive paddle or cellophane tape. This condition can present with severe pruritus but does not cause verrucous lesions.

(Choice B) Colonoscopy with terminal ileoscopy is used to evaluate for ileocolonic Crohn disease. Patients commonly have perianal involvement, but typical findings include painful abscesses and draining fistulae.

(Choice C) Condylomata lata are a manifestation of secondary syphilis, which can be confirmed by direct

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fistulae.

(Choice C) Condylomata lata are a manifestation of secondary syphilis, which can be confirmed by direct visualization of *Treponema pallidum* on darkfield microscopy of the tissue or exudate. Although condylomata lata may present as verruciform lesions resembling AGW, biopsy typically reveals a dense lymphoplasmacytic infiltrate.

(Choice D) Portal hypertension can lead to dilation of peripheral portosystemic collaterals. Involvement of the rectal submucosal veins (connecting the inferior mesenteric and iliac systems) can cause rectal varices, which present as enlarged veins resembling internal hemorrhoids. External verrucae are more consistent with AGW.

Educational objective:
Condylomata acuminata (anogenital warts) present as pink- or skin-colored plaques, papules, and verrucous lesions on the genitalia, perineum, or perianal skin; they are caused by human papillomavirus, primarily types 6 and 11. These lesions are associated with increased risk for HIV infection, and HIV testing is recommended.

References

- Condylomata acuminata (anogenital warts) contain accumulations of HIV-1 target cells that may provide

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A diarrheal outbreak is reported at a private school in Columbus, Ohio. Six healthy children age 10-11 and two teachers developed acute vomiting and diarrhea within a 2-day period. They describe the diarrhea as watery and without blood or mucus. Three of those affected are febrile during their illness. None of the patients have traveled abroad recently, and all are up to date with their vaccinations. Stool test results are pending. Which of the following pathogens is the most likely cause of the illness?

A. Adenovirus
B. *Campylobacter jejuni*
C. *Clostridioides* (formerly *Clostridium*) *difficile*
D. Enterotoxigenic *Escherichia coli*
E. Norovirus
F. Rotavirus
G. *Salmonella typhi*

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A diarrheal outbreak is reported at a private school in Columbus, Ohio. Six healthy children age 10-11 and two teachers developed acute vomiting and diarrhea within a 2-day period. They describe the diarrhea as watery and without blood or mucus. Three of those affected are febrile during their illness. None of the patients have traveled abroad recently, and all are up to date with their vaccinations. Stool test results are pending. Which of the following pathogens is the most likely cause of the illness?

- A. Adenovirus (4%)
- B. *Campylobacter jejuni* (1%)
- C. *Clostridioides* (formerly *Clostridium*) *difficile* (1%)
- D. Enterotoxigenic *Escherichia coli* (4%)
- ✓ E. Norovirus (64%)
- F. Rotavirus (23%)
- G. *Salmonella typhi* (1%)

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Norovirus	
Epidemiology	• Single-stranded RNA genome • Most common cause of viral gastroenteritis in developed countries
Clinical features	• Acute onset; resolves in 2-3 days • Vomiting &/or diarrhea (no blood or mucus)

Norovirus is the most common cause of **viral gastroenteritis**. Symptoms include diarrhea, **vomiting**, fever, malaise, and headache. The **diarrhea** is typically **watery without blood or mucus** due to lack of small bowel inflammation.

Norovirus (part of the *Calicivirus* family) possesses a linear, nonenveloped, single-stranded RNA genome. It is resistant to inactivation by acid, bile, and pancreatic enzymes. As a result, norovirus is easily transmitted via **fecal-oral spread** (eg, foodborne, person-to-person via contaminated bodily fluids) and results in **outbreaks** in crowded settings (eg, schools, hospitals, cruise ships, nursing homes). The incubation period is 1-2 days; symptoms develop acutely and self-resolve within days. The diagnosis is typically based solely on clinical presentation, but polymerase chain reaction testing may be performed to confirm an outbreak.

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(Choice A) Adenoviral gastroenteritis typically presents with fever and watery diarrhea. Outbreaks can occur, but these are far less common than with norovirus. Adenovirus more commonly causes pharyngoconjunctivitis and coryza (eg, runny nose, nasal congestion).

(Choice B) Vomiting, high fever, and bloody diarrhea are typical of *Campylobacter jejuni* enteritis. Transmission occurs via oral contact with contaminated food (eg, poultry) or drinks. Outbreaks are not as common as those of viral etiology.

(Choice C) *Clostridioides* (formerly *Clostridium*) *difficile* infection can result in asymptomatic carriers, pseudomembranous colitis, or fulminant colitis. Patients have watery diarrhea with or without blood, abdominal pain, fever, and leukocytosis. Prior antibiotic exposure (eg, fluoroquinolones, clindamycin) is the most significant risk factor.

(Choice D) Enterotoxigenic *Escherichia coli* (ETEC), the most common cause of traveler's diarrhea, is prevalent in developing countries. Although the acute onset of nausea, vomiting, and watery nonbloody diarrhea is typical of ETEC infection, it would be unlikely in patients who have not traveled abroad recently.

(Choice F) Gastroenteritis outbreaks can also occur with rotavirus infection, with a presentation similar to that of norovirus. However, the prevalence of rotavirus in developed countries has decreased dramatically since the introduction of routine childhood vaccination. Rotavirus is unlikely in vaccinated children (as in

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prevalent in developing countries. Although the acute onset of nausea, vomiting, and watery nonbloody diarrhea is typical of ETEC infection, it would be unlikely in patients who have not traveled abroad recently.

(Choice F) Gastroenteritis outbreaks can also occur with rotavirus infection, with a presentation similar to that of norovirus. However, the prevalence of rotavirus in developed countries has decreased dramatically since the introduction of routine childhood vaccination. Rotavirus is unlikely in vaccinated children (as in this case).

(Choice G) *Salmonella typhi* infection can result in typhoid fever and presents with fever, followed by abdominal pain and diarrhea and/or constipation. Severe complications (eg, hepatosplenomegaly, intestinal perforation, sepsis) occur in a minority of patients.

Educational objective:

Norovirus is the most common cause of viral gastroenteritis. Outbreaks in crowded settings (eg, schools, cruise ships, nursing homes) are common, and symptoms include vomiting and watery diarrhea.

References

- The burden of norovirus gastroenteritis: an important foodborne and healthcare-related infection.
- Evolution of norovirus.

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An 8-year-old boy is brought to the emergency department due to 2 days of fever, abdominal pain, and diarrhea. The patient has no significant medical history and has received all recommended vaccinations. He attends a primary school and has not traveled recently. The family recently brought home a new puppy from a kennel. The patient's stool is positive for occult blood but negative for ova and parasites. Which of the following is the most likely cause of this patient's symptoms?

A. *Bacillus cereus*
B. *Campylobacter*
C. *Giardia lamblia*
D. Norovirus
E. *Staphylococcus aureus*
F. *Vibrio parahaemolyticus*

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An 8-year-old boy is brought to the emergency department due to 2 days of fever, abdominal pain, and diarrhea. The patient has no significant medical history and has received all recommended vaccinations. He attends a primary school and has not traveled recently. The family recently brought home a new puppy from a kennel. The patient's stool is positive for occult blood but negative for ova and parasites. Which of the following is the most likely cause of this patient's symptoms?

A. *Bacillus cereus* (4%)
B. *Campylobacter* (58%)
C. *Giardia lamblia* (6%)
D. Norovirus (17%)
E. *Staphylococcus aureus* (1%)
F. *Vibrio parahaemolyticus* (11%)

Correct

58%
Answered correctly

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Campylobacter jejuni is a motile, curved, gram-negative rod that is a leading cause of gastroenteritis. The pathogen resides in the gastrointestinal tract of warm-blooded animals and is primarily transmitted to humans due to ingestion of contaminated food, particularly undercooked poultry. However, direct contact with **domesticated animals** (eg, dogs) is another important source of transmission; puppies from kennels are especially likely to harbor the bacteria.

Following ingestion, *Campylobacter* colonizes the intestinal mucosa, enters enterocytes within endocytic vacuoles, and causes cytotoxic injury due to specific virulence factors (eg, cytolethal distending toxin, lipooligosaccharide). Patients typically develop fever, crampy abdominal pain, and watery **diarrhea** that may be bloody. Stool studies will show **inflammation** (leukocytes, erythrocytes) but no ova or parasites; stool culture is diagnostic (enriched media at 42 C [107.6 F] and microaerophilic conditions). Manifestations usually resolve spontaneously in 3-5 days. In a minority of cases, the host response to *Campylobacter* infection generates cross-reacting antibodies to peripheral nerve myelin gangliosides, leading to Guillain-Barré syndrome.

(Choices A and E) *Bacillus cereus* and *Staphylococcus aureus* cause enterotoxin-mediated food-borne illness. Ingestion of the preformed toxin leads to rapid-onset nausea, vomiting, and abdominal pain (diarrhea can occur but is usually mild). *S aureus* food-borne illness is often linked to precooked foods,

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dairy products, custards, and mayonnaise-based salads; *B cereus* food-borne illness is often associated with starch-based foods, such as reheated rice.

(Choice C) *Giardia lamblia* is usually transmitted by drinking contaminated water. Foodborne or person-to-person spread may also occur. Giardia typically causes foul-smelling, watery diarrhea that is noninflammatory; therefore, no fecal blood or leukocytes are typically present. In addition, stool ova and parasite testing often reveals *Giardia* trophozoites or cysts.

(Choice D) Norovirus is the most common cause of viral gastroenteritis and is usually transmitted due to food or water contaminated with human feces. Patients typically develop a vomiting-predominant illness with abdominal pain and a moderate amount of watery diarrhea. However, the pathogen is noninflammatory and therefore no stool blood or leukocytes are seen.

(Choice F) *Vibrio parahaemolyticus* lives in marine environments and is typically transmitted via contaminated seafood (eg, shellfish). Manifestations include a diarrhea-predominant gastroenteritis. Life-threatening sepsis can occur in those with liver disease or hemachromatosis.

Educational objective:

Campylobacter infection is a common cause of gastroenteritis and is typically acquired from contaminated food (eg, undercooked poultry) or domesticated animals (eg, household dogs). Manifestations usually

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to-person spread may also occur. Giardia typically causes foul-smelling, watery diarrhea that is noninflammatory; therefore, no fecal blood or leukocytes are typically present. In addition, stool ova and parasite testing often reveals *Giardia* trophozoites or cysts.

(Choice D) Norovirus is the most common cause of viral gastroenteritis and is usually transmitted due to food or water contaminated with human feces. Patients typically develop a vomiting-predominant illness with abdominal pain and a moderate amount of watery diarrhea. However, the pathogen is noninflammatory and therefore no stool blood or leukocytes are seen.

(Choice F) *Vibrio parahaemolyticus* lives in marine environments and is typically transmitted via contaminated seafood (eg, shellfish). Manifestations include a diarrhea-predominant gastroenteritis. Life-threatening sepsis can occur in those with liver disease or hemachromatosis.

Educational objective:
Campylobacter infection is a common cause of gastroenteritis and is typically acquired from contaminated food (eg, undercooked poultry) or domesticated animals (eg, household dogs). Manifestations usually include fever, cramping abdominal pain, and watery diarrhea that may be bloody. Stool studies typically show blood and leukocytes. *Campylobacter* infection is associated with Guillain-Barré syndrome.

Microbiology Infectious Diseases Acute diarrhea

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A 37-year-old man is brought to the emergency department following a motor vehicle accident in which he was the unrestrained driver. Paramedics report that his breath smelled of alcohol at the scene. En route to the hospital, the patient receives 2 L intravenous normal saline. In the emergency department, his blood pressure is 100/60 mm Hg, pulse is 130/min, and respirations are 44/min. He is admitted directly to the intensive care unit, where he is intubated and placed on mechanical ventilation. A decision is made to insert a central venous catheter. In addition to sterile draping during the procedure, which of the following actions would be most likely to prevent intravascular catheter-related infections?

A. Alcohol-based hand scrub prior to beginning the procedure
B. Daily application of topical mupirocin at the catheter site
C. Insertion of the catheter in the femoral vein
D. One dose of intravenous vancomycin prior to catheter insertion
E. Replacement of the catheter every 7 days

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A 37-year-old man is brought to the emergency department following a motor vehicle accident in which he was the unrestrained driver. Paramedics report that his breath smelled of alcohol at the scene. En route to the hospital, the patient receives 2 L intravenous normal saline. In the emergency department, his blood pressure is 100/60 mm Hg, pulse is 130/min, and respirations are 44/min. He is admitted directly to the intensive care unit, where he is intubated and placed on mechanical ventilation. A decision is made to insert a central venous catheter. In addition to sterile draping during the procedure, which of the following actions would be most likely to prevent intravascular catheter-related infections?

- A. Alcohol-based hand scrub prior to beginning the procedure (46%)
- B. ~~Daily application of topical mupirocin at the catheter site~~ (9%)
- C. ~~Insertion of the catheter in the femoral vein~~ (1%)
- D. ~~One dose of intravenous vancomycin prior to catheter insertion~~ (12%)
- E. ~~Replacement of the catheter every 7 days~~ (29%)

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Central venous catheters (CVCs) are commonly used for hemodynamic monitoring and administration of fluids and medications in critically ill patients. **Infection** originating from the patient's skin flora or bacteria on the hands of health care workers is one of the major complications of CVCs. **Gram-positive cocci**, primarily coagulase-negative staphylococci and *Staphylococcus aureus*, account for the majority of these infections.

The Centers for Disease Control and Prevention recommend the following steps to reduce CVC infections:

- **Hand hygiene** with an alcohol sanitizer or soap and water prior to donning sterile gloves
- Maximal **barrier precautions** during insertion (surgical mask, sterile gloves, long-sleeved surgical gown, and a large sterile sheet drape)
- Preparation of the insertion site with chlorhexidine antiseptic
- Use of subclavian or internal jugular insertion sites (femoral vein has a higher risk of infection) **(Choice C)**
- Prompt removal of the catheter when it is no longer needed

(Choice B) Topical antimicrobial ointments do not reduce the rate of CVC-related infections and are associated with increased risk of antimicrobial resistance and *Candida* colonization.

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(Choice D) Oral or parenteral antibiotics have not been found to reduce the incidence of CVC-related infections. In addition, the prophylactic use of vancomycin has been found to increase the risk of vancomycin-resistant enterococcus.

(Choice E) Catheter replacement at scheduled intervals does not reduce infection rates. Routine replacement of CVCs is not necessary for functional catheters with no evidence of infection.

Educational objective:

The most important steps for prevention of central venous catheter infections are as follows:

- Proper hand hygiene
- Full barrier precautions during insertion
- Chlorhexidine skin disinfection
- Avoidance of the femoral insertion site
- Removal of the catheter when it is no longer needed

References

- Beyond the bundle--journey of a tertiary care medical intensive care unit to zero central line-associated bloodstream infections.

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Researchers develop a novel drug to treat HIV infection. In an in vitro experiment, wild-type viral isolates are cultured with human CD4 T lymphocytes in the presence of the drug. Microscopic evaluation of these cells reveals no cytopathic changes, and no intracellular viral particles can be detected. Further analysis reveals that in the presence of the drug the virus attaches to the cellular membrane, but fusion of the viral and cell membranes does not occur. Which of the following is the most likely target of this medication?

A. Viral integrase enzyme
B. Viral *Nef* gene product
C. Viral *Tat* gene product
D. T-cell antigen receptor-CD3 complex
E. T-cell chemokine receptor
F. T-cell CTLA4 (CD152)

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Researchers develop a novel drug to treat HIV infection. In an in vitro experiment, wild-type viral isolates are cultured with human CD4 T lymphocytes in the presence of the drug. Microscopic evaluation of these cells reveals no cytopathic changes, and no intracellular viral particles can be detected. Further analysis reveals that in the presence of the drug the virus attaches to the cellular membrane, but fusion of the viral and cell membranes does not occur. Which of the following is the most likely target of this medication?

A. ~~Viral integrase enzyme~~ (13%)
B. Viral *Nef* gene product (13%)
C. Viral *Tat* gene product (6%)
D. ~~T-cell antigen receptor-CD3 complex~~ (17%)
E. T-cell chemokine receptor (24%)
F. ~~T-cell CTLA4 (CD152)~~ (23%)

Correct

24%
Answered correctly

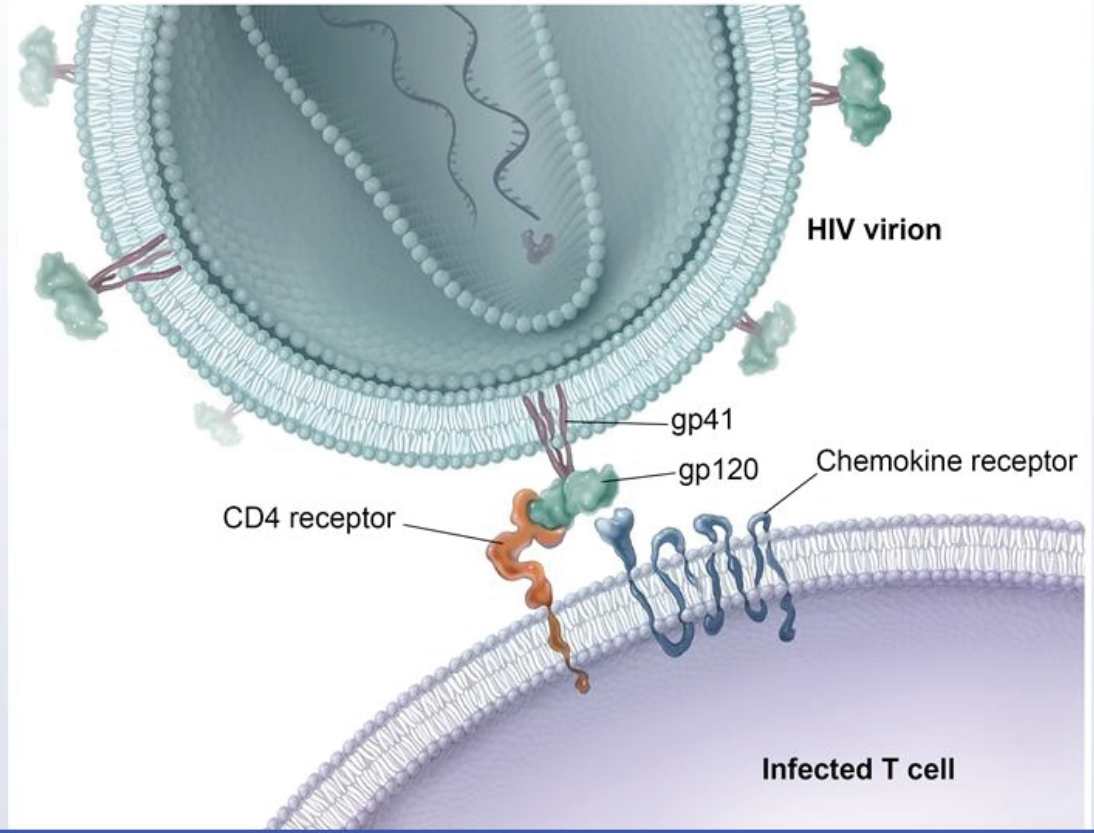
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HIV attaches to host cells using the viral surface glycoprotein **gp120**. This glycoprotein **binds to the CD4** molecule as the primary receptor and the **chemokine receptor CCR5** (or CXCR4) as a coreceptor. Binding of the primary receptor and coreceptor induces a conformational change in gp120 that exposes the underlying transmembrane glycoprotein **gp41**, which **mediates viral fusion** to the host cell and release of the viral capsid into the cytoplasm.

The drug described in this case does not interfere with viral attachment but does interfere with viral fusion. This implies that gp120 is still able to bind to the primary CD4 receptor but may be blocked from binding to the chemokine coreceptor, which would prevent the conformational change to gp120 required for viral fusion. **Chemokine receptor antagonists** (eg, maraviroc) block this step in the HIV replication cycle. The drug described in this case could also be a fusion inhibitor (eg, enfuvirtide), which blocks gp41 from fusing the viral and host plasma membranes.

(Choices B and C) *Nef* and *tat* are HIV regulatory genes. The *nef* gene product downregulates the expression of class I major histocompatibility complex proteins on the surface of infected cells, which limits immune recognition by cytotoxic T cells. The *tat* gene product is a transcriptional activator that promotes viral gene expression.

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HIV regulatory & accessory proteins	
Tat	Promotes transcription of viral genes
Rev	Enhances export of unspliced viral transcripts from nucleus to cytoplasm
Nef	Downregulates host CD4 & MHC I proteins (inhibits immune recognition)
Vpu	Aids viral assembly & release
Vpr	Facilitates nuclear entry & inhibits host cell division
Vif	Increases infectivity & viral yield

MHC = major histocompatibility complex.

New | Existing

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immune recognition by cytotoxic T cells. The *tat* gene product is a transcriptional activator that promotes viral gene expression.

(Choice A) HIV integrase is a viral enzyme that inserts the viral cDNA into the host cell chromosome.

(Choice D) The CD3 receptor is found on the surface of mature T lymphocytes. Monoclonal antibodies against CD3 are being investigated for autoimmune disorders, but this receptor does not play a role in HIV entry.

(Choice F) CTLA4 (CD-152) is a negative regulator of T-cell activation. Antagonists of CTLA4 are used as immune checkpoint inhibitors in cancer therapy (eg, melanoma).

Educational objective:
The chemokine receptor CCR5 is a coreceptor that enables the HIV virus to enter cells. Blockade of CCR5 by chemokine receptor antagonists prevents viral entry into host cells.

Microbiology	Infectious Diseases	HIV
Subject	System	Topic

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A 29-year-old woman comes to the hospital due to fever and skin rash. She returned from a trip to Brazil 10 days ago. Her symptoms started 5 days ago with a headache, retro-orbital pain, high-grade fever, and joint and muscle pains. She has also had an episode of epistaxis. Today, she noticed a skin rash all over her body. Examination shows a diffuse maculopapular rash and scattered petechiae. Laboratory study results show thrombocytopenia. Her boyfriend traveled to Brazil with her and is asymptomatic.

Transmission of the pathogen causing this patient's current symptoms occurs in a manner that is most similar to which of the following diseases?

A. Chikungunya fever
B. Lymphogranuloma venereum
C. Meningococcal meningitis
D. Pulmonary tuberculosis
E. Rocky Mountain spotted fever
F. Typhoid fever

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10 days ago. Her symptoms started 5 days ago with a headache, retro-orbital pain, high-grade fever, and joint and muscle pains. She has also had an episode of epistaxis. Today, she noticed a skin rash all over her body. Examination shows a diffuse maculopapular rash and scattered petechiae. Laboratory study results show thrombocytopenia. Her boyfriend traveled to Brazil with her and is asymptomatic. Transmission of the pathogen causing this patient's current symptoms occurs in a manner that is most similar to which of the following diseases?

- A. Chikungunya fever (69%)
- B. Lymphogranuloma venereum (1%)
- C. Meningococcal meningitis (4%)
- D. Pulmonary tuberculosis (1%)
- E. Rocky Mountain spotted fever (17%)
- F. Typhoid fever (5%)

Correct

69%

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Transmission of common infections	
Mechanism of transmission	**Examples**
Direct contact	• Infectious mononucleosis • Lymphogranuloma venereum • RSV, rhinovirus, Norwalk virus
Droplet (>5 µm) (eg, coughing, sneezing)	• Influenza • Meningococcus • Adenovirus, pertussis
Airborne (<5 µm) (eg, aerosols, ventilation system)	• TB • Measles, chickenpox, smallpox
Vectorborne	• Mosquitoes (malaria, dengue fever, chikungunya) • Ticks (Lyme disease, RMSF)

RMSF = Rocky Mountain spotted fever; **RSV** = respiratory syncytial virus; **TB** = tuberculosis.

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This patient's presentation after recent travel to Brazil is consistent with **dengue fever (DF)**. DF is due to a virus transmitted by the *Aedes aegypti* **mosquito**. It is prevalent in tropical and subtropical regions (South and Southeast Asia, Pacific Islands, Caribbean, Americas). DF presents as an acute febrile illness with headache, **retro-orbital pain**, and joint and muscle pain. Other findings can include **hemorrhage** (eg, petechiae, purpura, epistaxis, melena), thrombocytopenia, leukopenia, and hemoconcentration.

The *Aedes* mosquito also transmits the virus causing **chikungunya**, a febrile illness with flulike symptoms, prominent polyarthralgia/arthritis (hands, wrists, ankles), and diffuse macular rash. As a result, many areas have had **simultaneous outbreaks** of both dengue and chikungunya. Preventive measures against both infections include protective barriers (eg, bed nets, window screens) and insect spraying.

(Choice B) Lymphogranuloma venereum can be caused by direct sexual contact with an infected individual.

(Choice C) Meningococcal meningitis is acquired by droplet contact. In a health care setting, measures to prevent transmission include wearing a face mask within 3 feet of the patient (who is typically placed in a private room).

(Choice D) Pulmonary tuberculosis is usually spread through airborne contact. Patients are placed in a

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(Choice C) Meningococcal meningitis is acquired by droplet contact. In a health care setting, measures to prevent transmission include wearing a face mask within 3 feet of the patient (who is typically placed in a private room).

(Choice D) Pulmonary tuberculosis is usually spread through airborne contact. Patients are placed in a negative-pressure isolation room, and specific respirator masks are worn by all contacts and visitors.

(Choice E) Rocky Mountain spotted fever is due to *Rickettsia rickettsii*, which is transmitted by ticks rather than mosquitoes.

(Choice F) Typhoid fever is caused by *Salmonella* and is usually acquired from contaminated food or water, typically in areas with poor sanitation.

Educational objective:

The *Aedes aegypti* mosquitoes can transmit the viruses that cause dengue fever and chikungunya. Classic dengue fever presents as an acute febrile illness with headache, retro-orbital pain, and joint and muscle pain. Chikungunya is a febrile illness with flulike symptoms, prominent polyarthralgias, and diffuse macular rash.

References

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A 43-year-old man comes to the emergency department due to fever, chest pain, and hemoptysis. He has a history of a hematologic malignancy for which he recently underwent a cycle of chemotherapy. Laboratory studies show neutropenia due to the chemotherapeutic agents. A nodule with surrounding hypoattenuation is revealed on chest CT. Galactomannan and beta-D-glucan assays are elevated. Sputum cultures grow *Aspergillus*. The patient is placed on intravenous amphotericin B. During the infusion, he develops headaches, rigors, and hypotension. Over the next few days, there is a decline in renal function attributed to amphotericin. These toxic effects are likely due to binding of the antifungal agent to which of the following?

A. Cell membrane cholesterol
B. Cytochrome P450
C. Microtubular proteins
D. Mitochondrial enzymes
E. Ribosomal subunit

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www.ncbi.nlm.nih.gov/pubmed/23497591

a history of a hematologic malignancy for which he recently underwent a cycle of chemotherapy. Laboratory studies show neutropenia due to the chemotherapeutic agents. A nodule with surrounding hypoattenuation is revealed on chest CT. Galactomannan and beta-D-glucan assays are elevated. Sputum cultures grow *Aspergillus*. The patient is placed on intravenous amphotericin B. During the infusion, he develops headaches, rigors, and hypotension. Over the next few days, there is a decline in renal function attributed to amphotericin. These toxic effects are likely due to binding of the antifungal agent to which of the following?

- A. Cell membrane cholesterol (75%)
- B. ~~Cytochrome P450~~ (7%)
- C. ~~Microtubular proteins~~ (9%)
- D. ~~Mitochondrial enzymes~~ (4%)
- E. Ribosomal subunit (3%)

Correct

75%

02 mins, 01 sec

10/04/2020

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This patient with febrile neutropenia following chemotherapy has invasive aspergillosis (fever, chest pain, hemoptysis, chest imaging showing nodule with hypoattenuation consistent with "halo sign").

Amphotericin B is a mainstay of treatment for many systemic mycoses. It preferentially binds the **ergosterol** of fungal cell membranes, leading to fungal cell lysis. This drug is relatively selective as it has a higher affinity for ergosterol (in fungal membranes) than for cholesterol (in human cell membranes). However, it binds **cholesterol** to a degree, which explains a large number of its adverse effects.

Amphotericin B is often administered intravenously. Its main toxicities include the following:

- **Acute infusion-related reactions**, such as fever, chills, rigors, and hypotension, can occur. These are common and are seen most frequently during initial infusions (often diminish with subsequent infusions). Premedication with antipyretics and antihistamines can lessen the severity of these effects.
- **Dose-dependent nephrotoxicity** can result from a drug-induced decrease in the glomerular filtration rate. Permanent loss of renal function is thought to be related to the cumulative total dose. Renal function (eg, creatinine) should be closely monitored in patients undergoing treatment with amphotericin. Concomitant administration of other nephrotoxic drugs (eg, aminoglycosides, cyclosporine) should be avoided.
- Significant **electrolyte abnormalities** (hypomagnesemia and hypokalemia) can develop. These

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- Significant **electrolyte abnormalities** (hypomagnesemia and hypokalemia) can develop. These effects occur in the majority of patients within the first week of therapy. Electrolytes should be monitored daily and replaced as needed.
- **Anemia** occurs due to suppression of renal erythropoietin synthesis. This effect may be severe in patients with HIV who are taking zidovudine (which also suppresses bone marrow function).
- **Thrombophlebitis** can be seen at the site of injection.

(Choice B) Triazole antifungals (eg, fluconazole, itraconazole) inhibit cytochrome P450 enzymes, suppressing the metabolism of many other medications. This effect explains the myriad drug interactions of this group of antifungal agents.

(Choice C) Binding of microtubular proteins is the mechanism of griseofulvin, which is effective against dermatophytes only.

(Choices D and E) Amphotericin B does not interact with ribosomal subunits or mitochondrial enzymes.

Educational objective:
Amphotericin B binds the ergosterol of fungal cell membranes to exert its antifungal effects. However, it also binds cholesterol to some degree, causing toxicity to human tissues. The most important adverse effects of amphotericin B are nephrotoxicity, hypokalemia, and hypomagnesemia.

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A 53-year-old man comes to the emergency department due to 2 weeks of intermittent low-grade fevers and fatigue. Temperature is 38.5 C (101.3 F), blood pressure is 120/80 mm Hg, pulse is 92/min, and respirations are 16/min. On cardiovascular examination, an early diastolic murmur is present and best heard at the left sternal edge. Subungual splinter hemorrhages are seen. Laboratory study results show leukocytosis and an elevated erythrocyte sedimentation rate. Blood cultures are drawn and grow gram-positive cocci that synthesize dextrans from sucrose. The organism contributing to this patient's current condition is also associated with which of the following?

A. Anterior uveitis
B. Colon cancer
C. Dental caries
D. Erythema nodosum
E. Glomerulonephritis
F. Migratory polyarthritis

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and fatigue. Temperature is 38.5 C (101.3 F), blood pressure is 120/80 mm Hg, pulse is 92/min, and respirations are 16/min. On cardiovascular examination, an early diastolic murmur is present and best heard at the left sternal edge. Subungual splinter hemorrhages are seen. Laboratory study results show leukocytosis and an elevated erythrocyte sedimentation rate. Blood cultures are drawn and grow gram-positive cocci that synthesize dextrans from sucrose. The organism contributing to this patient's current condition is also associated with which of the following?

- A. Anterior uveitis (1%)
- B. Colon cancer (8%)
- ✓ C. Dental caries (72%)
- D. Erythema nodosum (4%)
- E. Glomerulonephritis (8%)
- F. Migratory polyarthritis (4%)

Correct

72%

01 min, 48 secs

10/24/2020

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Viridans streptococci, notably *Streptococcus mutans* and *S sanguinis*, are normally present in the human mouth and are major contributors to tooth decay and the initiation of **dental caries**. These organisms also cause bacterial **endocarditis**, deep wound infections, abdominal abscesses, and septicemia. Viridans streptococci can **adhere** to tooth enamel and to fibrin-platelet aggregates on damaged heart valves due to their ability to produce insoluble extracellular polysaccharides (**dextrans**) using sucrose as a substrate. This colonization of host surfaces contributes to their ability to cause infection.

(Choice A) Anterior uveitis (inflammation of the iris) can be caused by infectious processes (eg, herpes viruses, syphilis, Lyme disease) and inflammatory conditions (eg, HLA-B27-related diseases, sarcoidosis). It is not associated with viridans streptococcal infections.

(Choice B) *S bovis* is associated with colon cancer, and patients with *S bovis* endocarditis should undergo colonoscopic evaluation to exclude neoplasia.

(Choice D) Erythema nodosum (erythematous to violaceous subcutaneous nodules usually appearing on the legs) is a nonspecific finding. It is associated with multiple bacterial infections, most commonly *S pyogenes* pharyngitis, but also *Staphylococcus aureus*, fungi (eg, coccidioidomycosis, histoplasmosis, blastomycosis), chlamydia, and others. It is also associated with Crohn disease, sarcoidosis, and other inflammatory conditions.

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pyogenes pharyngitis, but also *Staphylococcus aureus*, fungi (eg, coccidioidomycosis, histoplasmosis, blastomycosis), chlamydia, and others. It is also associated with Crohn disease, sarcoidosis, and other inflammatory conditions.

(Choices E and F) Poststreptococcal glomerulonephritis is a type III (immune complex-mediated) hypersensitivity reaction in which immune complexes deposit on the glomerular membrane and fix complement, leading to inflammation, renal dysfunction, hematuria, and nephritic range proteinuria. Migratory polyarthritis is a characteristic of rheumatic fever, an immune-mediated disease. These conditions typically follow infections with group A *Streptococcus* (*S pyogenes*), which does not produce dextrans.

Educational objective:
Viridans streptococci produce dextrans that aid them in colonizing host surfaces, such as dental enamel and heart valves. These organisms cause subacute bacterial endocarditis, classically in patients with preexisting cardiac valvular defects after dental manipulation.

Microbiology	Infectious Diseases	Endocarditis
Subject	System	Topic

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A 22-year-old woman comes to the office due to worsening cough. The patient has been coughing every day for the past several months, but over the last 4 weeks, the cough has worsened, with increased amounts of thick sputum and shortness of breath. Streaks of blood have been present in the sputum on several occasions. The patient also has a history of chronic sinusitis and repeated hospitalizations for airway infections. She takes pancreatic enzyme supplements for chronic diarrhea. She does not use tobacco, alcohol, or illicit drugs. Physical examination reveals nasal polyps, a barrel-shaped chest, bilateral coarse lung crackles, and digital clubbing. Chest x-ray shows hyperinflated lungs and dilated, thickened airways. Sputum culture from this patient is most likely to yield which of the following organisms?

A. *Aspergillus fumigatus*
B. *Moraxella catarrhalis*
C. *Mycobacterium tuberculosis*
D. *Pseudomonas aeruginosa*
E. *Streptococcus pneumoniae*

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A. *Aspergillus fumigatus* (9%)
B. *Moraxella catarrhalis* (6%)
C. *Mycobacterium tuberculosis* (3%)
D. *Pseudomonas aeruginosa* (68%)
E. *Streptococcus pneumoniae* (11%)

Correct

68%

01 min, 15 secs

02/19/2021

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Cystic fibrosis (CF) is a progressive, fatal illness characterized by the development of thick, viscous, clogging secretions in a multitude of organs. Young adults with CF typically have several manifestations of the disorder, including pancreatic insufficiency (eg, diarrhea), chronic sinusitis, nasal polyps, and chronic bronchitis (eg, long-standing productive cough, hyperinflated lungs, barrel chest). However, **persistent lower respiratory tract infection** is the major source of morbidity and death.

Early in the course of the disease, thick airway secretions obstruct mucociliary clearance and lead to the colonization of the lower respiratory tract with pathogenic bacteria. Although *Haemophilus influenzae* and *Staphylococcus aureus* are seen in children with CF, ***Pseudomonas aeruginosa*** is the major pathogen in **adults**. This organism forms a biofilm and switches to a mucoid phenotype to prevent its full elimination (even with antibiotics). Neutrophils respond by releasing elastase, myeloperoxidase, and reactive oxygen species, but these compounds are insufficient to clear the infection and progressively destroy the walls of the airway, leading to **bronchiectasis** and respiratory decline.

(Choice A) Allergic bronchopulmonary aspergillosis (ABPA) is a hypersensitivity reaction to *Aspergillus fumigatus* that primarily manifests with asthma-like symptoms. Although ABPA can occur in patients with CF, it is far less common than *Pseudomonas* lower respiratory infections.

(Choice B) *Moraxella catarrhalis* is an upper respiratory pathogen that frequently causes otitis media,

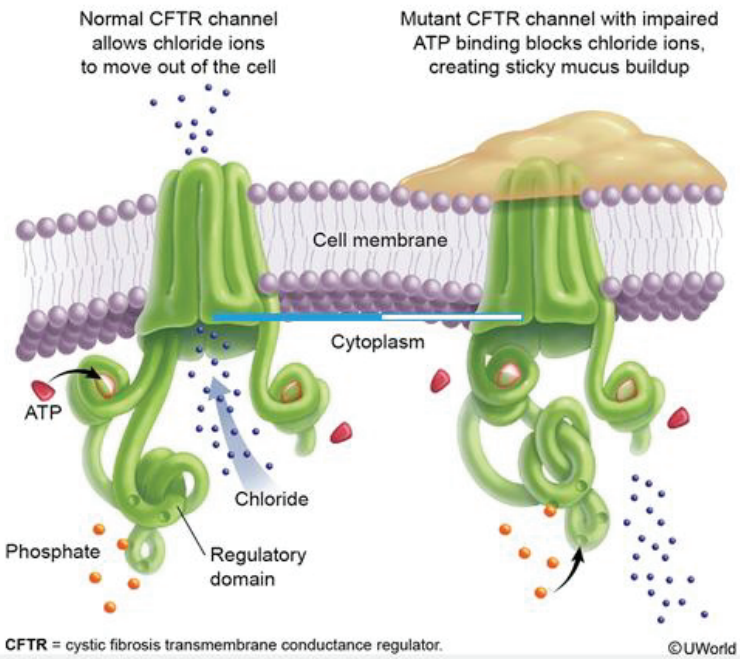
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Exhibit Display

Cystic fibrosis pathogenesis



CFTR = cystic fibrosis transmembrane conductance regulator.

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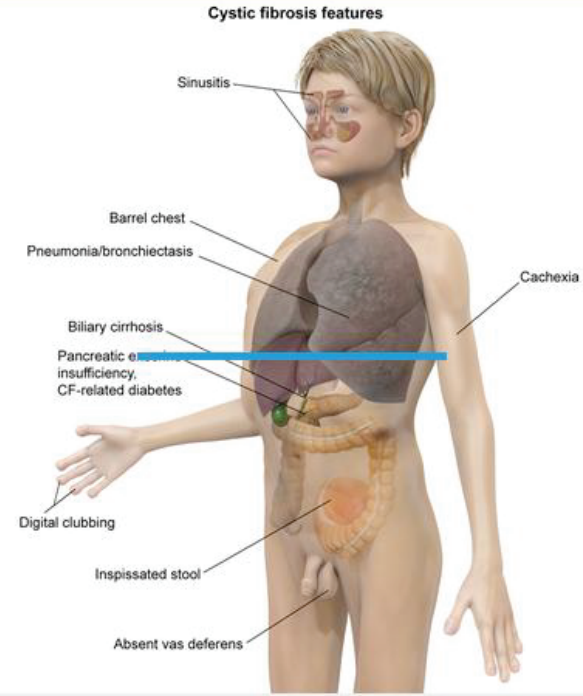
(Choice B) *Moraxella catarrhalis* is an upper respiratory pathogen that frequently causes otitis media,

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Exhibit Display



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(Choice B) *Moraxella catarrhalis* is an upper respiratory pathogen that frequently causes otitis media,

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(Choice B) *Moraxella catarrhalis* is an upper respiratory pathogen that frequently causes otitis media, sinusitis, bronchitis, and laryngitis. Although this organism is a common cause of exacerbations of chronic obstructive pulmonary disease, it is not a frequent colonizer of patients with CF.

(Choice C) *Mycobacterium tuberculosis* infections can cause coughing for several weeks or months and, occasionally, hemoptysis. However, thick sputum production is uncommon. In addition, chest x-ray typically reveals cavitary lesions in the upper lobes.

(Choice E) *Streptococcus pneumoniae* is the leading cause of community-acquired pneumonia and a frequent underlying pathogen in sinusitis, bronchitis, and otitis media. It is not a typical cause of persistent infection in patients with CF.

Educational objective:
In patients with cystic fibrosis, pathogenic bacteria colonize the respiratory tract early in the disease course. The leading pathogen in adults is *Pseudomonas aeruginosa*, which forms a thick biofilm to prevent its full elimination from the body.

Microbiology	Infectious Diseases	Cystic fibrosis
Subject	System	Topic

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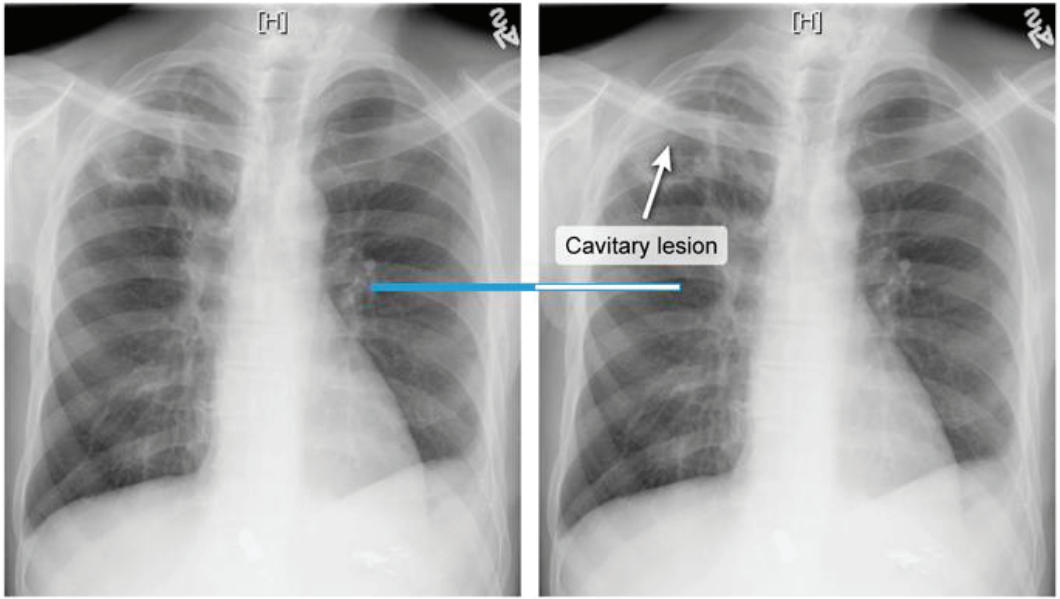
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(Choice B) *Moraxella catarrhalis* is an upper respiratory pathogen that frequently causes otitis media

Exhibit Display

Cavitary lung lesion



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The public health department of a developing country performs an epidemiologic study to assess the nationwide incidence of upper respiratory infections among children. The data show a high rate of childhood bacterial pharyngitis. Current practice guidelines indicate that a rapid test should be performed in children to identify the presence of bacterial antigens. If this test is negative, a throat culture, the gold standard for definitive diagnosis, is then performed. To offset cost and avoid losing patients to follow-up, the department is considering recommending the empiric use of penicillin for the treatment of suspected bacterial pharyngitis. Which of the following would be expected to decrease after long-term implementation of this guideline?

A. Deaths associated with diarrheal illness
B. Diagnoses of serum sickness-like reactions
C. Incidence of nephritic syndrome
D. Need for cardiac surgery
E. Use of broad-spectrum antibiotics

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A. Deaths associated with diarrheal illness (2%)
B. Diagnoses of serum sickness-like reactions (2%)
C. Incidence of nephritic syndrome (30%)
D. Need for cardiac surgery (53%)
E. Use of broad-spectrum antibiotics (10%)

Correct

53%
Answered correctly

26 secs
Time Spent

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Acute rheumatic fever	
Epidemiology	• Endemic in developing countries
Pathogenesis	• Occurs 2-4 weeks after acute group A streptococcal pharyngitis • Molecular mimicry: Anti-streptococcal antibodies attack cardiac & neuronal antigens
Clinical features	• Acute/subacute ◦ Migratory arthritis ◦ Pancarditis (mitral regurgitation) ◦ Sydenham chorea • Chronic ◦ Mitral stenosis
Prevention	• Prompt treatment of streptococcal pharyngitis with penicillin

Early **penicillin** treatment of **group A streptococcal pharyngitis** is important for the **prevention of acute rheumatic fever** (ARF), a major cause of cardiovascular death in many developing nations. ARF primarily

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Early **penicillin** treatment of **group A streptococcal pharyngitis** is important for the **prevention of acute rheumatic fever** (ARF), a major cause of cardiovascular death in many developing nations. ARF primarily affects the heart and central nervous system because host antibodies produced in response to streptococcal antigens cross-react with host antigens in these organs. Chronic cardiac inflammation can progress to rheumatic heart disease, specifically valvular disease. The **mitral valve** is the most commonly affected and gradually thickens, fibroses, and calcifies, eventually requiring valvotomy or more invasive surgical intervention.

Empiric therapy for a condition must be considered in the context of the host characteristics, pre-test probability of the disease, benefits/risks of waiting for a definitive diagnosis, and cost of therapy versus its potential complications. If all cases of acute streptococcal pharyngitis were treated empirically, the incidence of rheumatic heart disease and associated cardiac procedures would likely decrease.

(Choice A) Antibiotic use can promote diarrhea by altering the gut microbial milieu. This alteration can lead to overgrowth of *Clostridium difficile*, a gram-positive bacterium that can cause profuse, watery diarrhea and life-threatening fulminant colitis. Therefore, increasing antibiotic use would likely result in increased diarrheal illness and potential complications.

(Choice B) Serum sickness-like reactions are associated with certain infections (eg, hepatitis B) and

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(Choice B) Serum sickness-like reactions are associated with certain infections (eg, hepatitis B) and antibiotics (eg, penicillin). The development of circulating drug-specific immune complexes may cause fever, rash, and arthritis. If penicillin was used more frequently, serum sickness-like reactions would potentially increase, not decrease.

(Choice C) Post-streptococcal glomerulonephritis (PSGN) is the most common cause of nephritic syndrome in children worldwide. It is caused by deposition of immune complexes in glomeruli following pharyngitis or skin infections with group A *Streptococcus*. Although early antibiotics are effective in preventing ARF, they have not been shown to reduce the risk of PSGN.

(Choice E) Empiric use of potentially unnecessary antibiotics may cause an increase in antibiotic resistance, thereby increasing the need for broad-spectrum antibiotics. For example, methicillin-resistant *Staphylococcus aureus* (MRSA) evolved from methicillin-sensitive *S aureus* via alteration of the protein binding site for beta-lactam antibiotics. As a result, broad-spectrum antibiotics (eg, vancomycin, daptomycin) are required for MRSA infections.

Educational objective:
Acute rheumatic fever is a complication of untreated group A streptococcal pharyngitis. Rheumatic heart disease is the most common cause of acquired valvular heart disease and cardiovascular death in developing countries. The incidence of acute rheumatic fever and rheumatic heart disease has been

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Educational objective:

Acute rheumatic fever is a complication of untreated group A streptococcal pharyngitis. Rheumatic heart disease is the most common cause of acquired valvular heart disease and cardiovascular death in developing countries. The incidence of acute rheumatic fever and rheumatic heart disease has been reduced in industrialized nations with prompt treatment of streptococcal pharyngitis with penicillin.

References

- Primary prevention of acute rheumatic fever and rheumatic heart disease with penicillin in South African

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A 22-year-old woman participates in a research study. She is asymptomatic and has not had a respiratory illness in the last 8 weeks. She reports no chronic medical problems and takes no medications. A nasopharyngeal specimen is obtained and cultured on a selective medium containing vancomycin, colistin, nystatin, and trimethoprim. The organism most likely to be isolated is typically associated with which of the following conditions?

- A. Cystitis
- B. Dental caries
- C. Diphtheria
- D. Meningitis
- E. Otitis media
- F. Pneumonia
- G. Rheumatic heart disease

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- A. Cystitis (7%)
- B. Dental caries (7%)
- C. Diphtheria (4%)
- ✓ D. Meningitis (57%)
- E. Otitis media (6%)
- F. Pneumonia (12%)
- G. Rheumatic heart disease (4%)

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Explanation

The nasopharynx is colonized with a wide range of gram-positive and gram-negative bacteria. Therefore, nasopharyngeal swabs are often cultured on media containing antibiotics to isolate a specific organism. The agar described in this case is the **Thayer-Martin medium**, used to identify pathogenic ***Neisseria* organisms** such as *N meningitidis* (a common cause of **meningitis**) and *N gonorrhoeae* (a common cause of urethritis). The Thayer-Martin medium is a chocolate sheep blood agar infused with vancomycin to inhibit gram-positive bacteria; with colistin and trimethoprim to inhibit gram-negative bacteria (other than pathogenic *Neisseria* species); and with nystatin to inhibit yeast.

(Choice A) The most common cause of cystitis is *Escherichia coli*, a gram-negative rod inhibited by colistin and trimethoprim. *E coli* is not a common nasopharyngeal organism.

(Choice B) Dental carries are caused primarily by *Streptococcus* (eg, *S mutans*) and *Lactobacillus* species, gram-positive organisms inhibited by vancomycin.

(Choice C) *Corynebacterium diphtheriae* is the cause of diphtheria. It usually presents with slow-onset sore throat, malaise, and low-grade fever. *C diphtheriae* is a gram-positive organism inhibited by vancomycin.

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sore throat, malaise, and low-grade fever. *C diphtheriae* is a gram-positive organism inhibited by vancomycin.

(Choices E and F) The most common cause of both otitis media and community-acquired pneumonia in adults is *Streptococcus pneumoniae*. Although *S pneumoniae* can colonize the nasopharynx, this gram-positive organism is inhibited by vancomycin.

(Choice G) Rheumatic heart disease is caused by *Streptococcus pyogenes* (group A streptococci), a common gram-positive pharyngeal pathogen. *S pyogenes* is inhibited by vancomycin.

Educational objective:

The Thayer-Martin medium is used to isolate pathogenic *Neisseria* species such as *N meningitidis* and *N gonorrhoeae*. It is a chocolate sheep blood agar that contains vancomycin to inhibit the growth of gram-positive organisms; colistin and trimethoprim to inhibit gram-negative bacteria (other than pathogenic *Neisseria*); and nystatin to inhibit yeasts.

References

- Cellular and molecular biology of Neisseria meningitidis colonization and invasive disease.

Microbiology Infectious Diseases Meningococci

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A 35-year-old man comes to the office due to 3 months of progressive swelling under his left jaw. The swelling spontaneously opened and drained pus a month ago but has not improved or resolved. The patient has no medical conditions other than dental caries; he had a tooth extracted prior to symptom onset. Physical examination shows an indurated, nontender mass in the left submandibular area with a small opening on the overlying skin. Gentle pressure on the mass yields thick pus containing sand/grain-like particles. The microbial pathogen with which of the following characteristics is the most likely cause of this patient's condition?

A. Bipolar-staining, gram-negative bacilli
B. Coagulase-producing, gram-positive cocci
C. Conidia-forming, dimorphic fungus
D. Filamentous, branching, gram-positive bacilli
E. Oxidase-positive, gram-negative bacilli

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A 35-year-old man comes to the office due to 3 months of progressive swelling under his left jaw. The swelling spontaneously opened and drained pus a month ago but has not improved or resolved. The patient has no medical conditions other than dental caries; he had a tooth extracted prior to symptom onset. Physical examination shows an indurated, nontender mass in the left submandibular area with a small opening on the overlying skin. Gentle pressure on the mass yields thick pus containing sand/grain-like particles. The microbial pathogen with which of the following characteristics is the most likely cause of this patient's condition?

A. ~~Bipolar-staining, gram-negative bacilli~~ (1%)

B. Coagulase-producing, gram-positive cocci (14%)

C. ~~Conidia-forming, dimorphic fungus~~ (1%)

✓ D. Filamentous, branching, gram-positive bacilli (77%)

E. ~~Oxidase-positive, gram-negative bacilli~~ (3%)

77%
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10/08/2020

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Cervicofacial *Actinomyces*	
Organism	• Gram-positive facultative/strict anaerobe • Branching & **filamentous growth** • Normal GI commensal
Pathophysiology	• Inoculated into submucosa (dental infection/**extraction**) → low oxygen tension → growth without regard to tissue planes
Manifestations	• Upper/lower jaw (**mandible)** • **Slowly progressive**, **nonpainful**, indurated mass • Sinus tracts with **sulfur granules** • Fever/lymphadenopathy are uncommon

GI = gastrointestinal.

Actinomyces are anaerobic, **gram-positive bacilli** that have a branching, filamentous growth pattern similar to the mycelial form of fungi (hence their "fungus-like" name). They exist as normal commensals of the human gastrointestinal tract and rarely cause illness. However, introduction of the bacteria into the

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Actinomyces are anaerobic, **gram-positive bacilli** that have a branching, filamentous growth pattern similar to the mycelial form of fungi (hence their "fungus-like" name). They exist as normal commensals of the human gastrointestinal tract and rarely cause illness. However, introduction of the bacteria into the submucosa during a mechanical trauma (eg, **tooth extraction**) can sometimes lead to invasive disease, particularly when the wound is associated with low oxygen tension (ie, due to necrosis or infection).

Infections with *Actinomyces* most commonly involve the **cervicofacial** region. The bacteria grow slowly and without regard to tissue planes, resulting in a chronic, nontender, **indurated perimandibular mass** that enlarges over time and evolves into multiple abscesses and **draining sinus tracts**. A characteristic finding is the presence of **sulfur granules**, yellow-orange granules in pus that resemble (but do not contain) sulfur. Sulfur granules are intertwined *Actinomyces* filaments mixed with necrotic tissue.

(Choice A) *Pasteurella multocida* is a gram-negative rod that exhibits bipolar staining (ends of bacilli stain more than the middle). This organism causes a rapidly progressive soft tissue infection following an animal (usually a cat) bite. Although *Pasteurella* infection may cause draining cutaneous sinus tracts, infections are acute and not associated with tooth extraction or sulfur granules.

(Choice B) *Staphylococcus aureus* is the leading cause of acute suppurative parotitis, which is associated with firm, erythematous swelling in the area of the mandibular angle. However, *S aureus* soft tissue

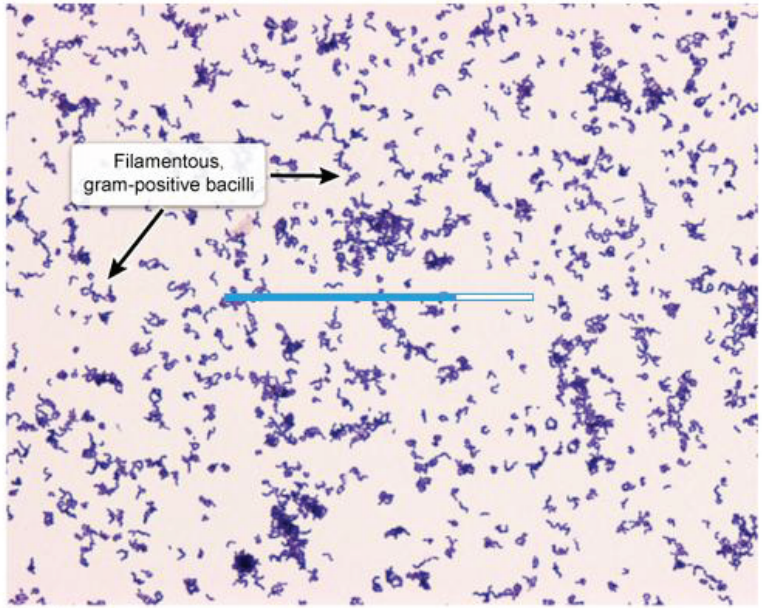
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Actinomyces are anaerobic, **gram-positive bacilli** that have a branching, filamentous growth pattern.

Exhibit Display

Actinomyces species



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abscesses progress rapidly and are painful and tender.

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(Choice B) *Staphylococcus aureus* is the leading cause of acute suppurative parotitis, which is associated with firm, erythematous swelling in the area of the mandibular angle. However, *S aureus* soft tissue abscesses progress rapidly and are painful and tender.

(Choice C) *Sporothrix schenckii* is a conidia-forming, dimorphic fungus that causes cutaneous sporotrichosis when contaminated soil is inoculated into skin or soft tissue. Manifestations include an ulcerating papule at the site of inoculation with proximal spread along the lymphatics leading to additional lesions.

(Choice E) *Pseudomonas* is an oxidase-positive, gram-negative bacillus that can produce a green pigment. Cutaneous *Pseudomonas* infections are most common after hot tub use and are usually associated with acute folliculitis (tender, pruritic papules or nodules).

Educational objective:

Actinomyces species are gram-positive, branching, filamentous bacteria that may cause cervicofacial infections when introduced to the submucosa during mechanical trauma (eg, tooth extraction). Manifestations include a slowly enlarging, nonpainful, chronic mandibular mass that evolves into multiple abscesses and sinus tracts draining yellow-orange sulfur granules.

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A 5-year-old girl is brought to the office by her mother due to 2 weeks of anorexia, nausea, epigastric discomfort, and loose bowel movements. She has had no fever or bloody stools. The patient recently returned from rural Brazil, where she spent the summer with family. She had no gastrointestinal symptoms during the trip but developed intensely pruritic eruptions between the toes of her right foot. The skin rash spontaneously resolved within a few days and was attributed to insect bites from walking barefoot in the fields. The patient has no prior medical conditions, takes no medications, and has received all age-appropriate vaccinations. On physical examination, the abdomen is soft and nontender with normoactive bowel sounds. Stool microscopy reveals smooth, thin-walled eggs. If left untreated, this patient's condition can lead to which of the following complications?

A. Chronic lymphedema
B. Dilated cardiomyopathy
C. Granulomatous endophthalmitis
D. Microcytic anemia
E. Vitamin B12 deficiency

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A. Chronic lymphedema (8%)
B. Dilated cardiomyopathy (11%)
C. Granulomatous endophthalmitis (5%)
D. Microcytic anemia (53%)
E. Vitamin B12 deficiency (20%)

Incorrect
Correct answer

53%

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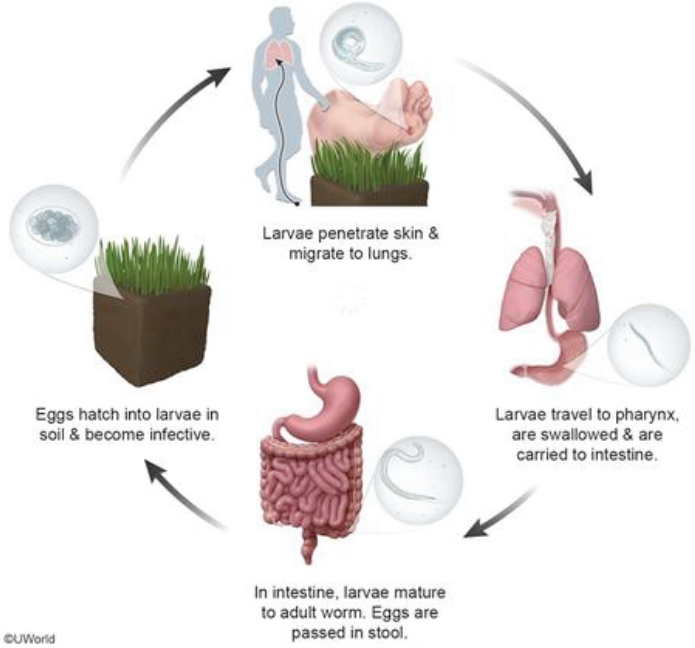
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Exhibit Display

Human hookworm life cycle



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Human hookworm infection is caused by *Necator americanus* and *Ancylostoma duodenale*. These pathogens are called hookworms because the head of the worm is often curved away from the body, giving the organism a "hooked" appearance. Most cases occur in **tropical and subtropical** regions where sanitation is poor. Transmission occurs when **egg-containing human feces** is deposited into shady, warm, moist soil, which allows the eggs to hatch into larvae. Spread occurs when larvae come into direct **contact with human skin** (eg, when walking barefoot).

Dermal penetration often results in a transient, pruritic, maculopapular or serpiginous rash at the entry site. The larvae then spread through the bloodstream to the lungs, where they rupture into the alveoli and are subsequently coughed up and swallowed. In the small intestine, the larvae mature into adults, attach to the gastrointestinal mucosa, and feed on human blood by lacerating capillaries. Because these organisms can live in the gastrointestinal tract for up to 14 years, total blood loss can be substantial. Therefore, the biggest risk of hookworm infection is iron-deficiency anemia **(microcytic anemia)** due to chronic blood loss.

Although many patients with hookworm infection are asymptomatic for months or years, some individuals develop transient pulmonary symptoms (eg, cough) during pulmonary migration or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea) during gastrointestinal migration. Diagnosis is generally made when smooth, thin-walled hookworm eggs are identified by stool microscopy. Peripheral **eosinophilia** is

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develop transient pulmonary symptoms (eg, cough) during pulmonary migration or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea) during gastrointestinal migration. Diagnosis is generally made when smooth, thin-walled hookworm eggs are identified by stool microscopy. Peripheral **eosinophilia** is also an important diagnostic clue.

(Choice A) Lymphatic filariasis is a mosquito-borne illness caused by roundworms (eg, *Wuchereria bancrofti*). Most patients are infected in childhood and remain asymptomatic, but a minority develops chronic lymphedema, which may result in elephantiasis. Eggs are not present in stool; diagnosis is made by serology or by identifying worms in the lymphatic system.

(Choice B) Chagas disease is linked to dilated cardiomyopathy and is most common in Latin America. It is caused by the protozoa *Trypanosoma cruzi*. Transmission occurs during a triatomine bug bite. Although transient skin and gastrointestinal symptoms can occur during acute infection, eggs are not seen in the stool; diagnosis is made mostly by serology or by blood microscopy.

(Choice C) Toxocariasis is caused by infection with dog or cat roundworms. Migrating larva cause a significant eosinophilic granulomatous response that can result in ocular (endophthalmitis) and organ damage. Diagnosis is made by serology; the organism does not shed eggs in the gastrointestinal tract.

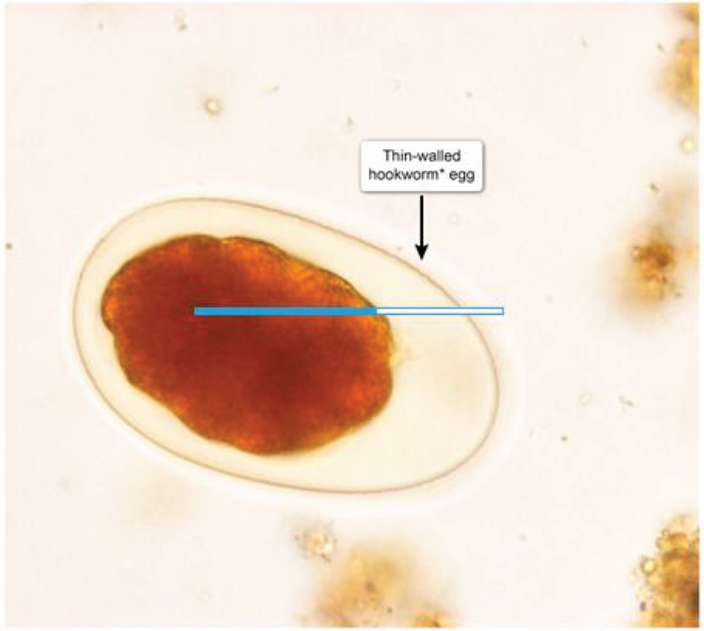
(Choice E) Diphyllobothriasis is caused by infection with a fish tapeworm and is classically linked with

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Exhibit Display

Hookworm egg



*Necator americanus and Ancylostoma duodenale

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[Choice E] Diphyllobothriasis is caused by infection with a fish tapeworm and is classically linked with

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significant eosinophilic granulomatous response that can result in ocular (endophthalmitis) and organ damage. Diagnosis is made by serology; the organism does not shed eggs in the gastrointestinal tract.

(Choice E) Diphyllobothriasis is caused by infection with a fish tapeworm and is classically linked with megaloblastic anemia due to vitamin B12 deficiency. Although the eggs can be seen on stool microscopy, they are distinguished by a lid-like opening (operculum). In addition, a transient skin rash would not be a feature of this disease.

Educational objective:

Hookworms are transmitted when human skin comes into contact with soil contaminated with human feces. The larvae penetrate the skin, travel to the lungs, are coughed up, and then subsequently swallowed. Adult hookworms live in the small intestine and feed on human blood. Therefore, chronic iron deficiency anemia (microcytic anemia) is the greatest complication.

References

- Soil-transmitted helminth infections.

Microbiology	Infectious Diseases	Intestinal helminth parasites
Subject	System	Topic

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A 24-year-old man comes to the emergency department due to severe nausea and vomiting 2 hours after a church picnic. He ate chicken salad that had been sitting out in the sun. The patient has no prior medical conditions. Temperature is 37.2 C (98.9 F), blood pressure is 126/84 mm Hg, and pulse is 86/min. No abdominal tenderness is present, and bowel sounds are normal. Blood cell counts and serum chemistry studies are within normal limits. Symptoms improve significantly within several hours with supportive care. Which of the following is the most likely cause of this patient's symptoms?

A. Bacterial exotoxin production in the gut
B. Bacterial invasion of the gut mucosa
C. Ingestion of preformed enterotoxin
D. Microbial attachment to the intestinal surface
E. Systemic absorption of luminal endotoxin

Submit

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A. Bacterial exotoxin production in the gut (9%)
B. Bacterial invasion of the gut mucosa (2%)
C. Ingestion of preformed enterotoxin (85%)
D. Microbial attachment to the intestinal surface (1%)
E. Systemic absorption of luminal endotoxin (1%)

Correct

85%
Answered correctly

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Major pathologic mechanisms of foodborne illness		
Enterotoxin ingested	*Staphylococcus aureus* *Bacillus cereus*	• **Quick onset** (1-6 hours) • **Vomiting** predominant
Enterotoxin made in intestine	*Clostridium perfringens* ETEC/STEC *Vibrio cholerae*	• **Delayed** onset (>1 day) • Watery/bloody **diarrhea**
Bacterial epithelial invasion	*Campylobacter jejuni* Nontyphoidal salmonella *Listeria monocytogenes*	• Variable onset • Watery/bloody **diarrhea** • **Fever** • Systemic illness (*Listeria*)

ETEC = enterotoxigenic *Escherichia coli*; **STEC** = Shiga toxin-producing *E coli*.

Enterotoxigenic *Staphylococcus aureus* is a leading cause of foodborne illness. This pathogen inoculates food during unsanitary preparation by an asymptomatic carrier. Storage of the food at room temperature for extended periods (eg, picnic, pot luck meal) allows the bacteria to proliferate and generate a heat-stable **enterotoxin**. Ingestion of the **preformed** toxin leads to **rapid-onset illness** that includes

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a heat-stable **enterotoxin**. Ingestion of the **preformed** toxin leads to **rapid-onset illness** that includes nausea, **vomiting**, and abdominal pain. Occasionally, mild fever and diarrhea may also be present. Symptoms resolve in a few hours with symptomatic care.

Because the disease is due to the ingestion of a preformed toxin, no person-to-person transmission occurs. However, outbreaks may arise when people eat the same contaminated food at an event or party. High risk foods include dairy products, produce, precooked meat, eggs, and mayonnaise-based **salads** (eg, chicken salad).

A similar clinical picture of rapid-onset nausea, vomiting, and abdominal cramping can be seen with food-borne illness due to *Bacillus cereus*, which also produces a heat-stable enterotoxin. *B cereus* characteristically contaminates starchy foods (eg, rice); illness is often associated with reheated rice.

(Choices A, B, and D) Foodborne illness can also be caused by other bacterial mechanisms, such as:

- Enterotoxin production within the intestine by enterotoxigenic *Escherichia coli* (ETEC) and *Vibrio cholera*, whose toxins cause watery diarrhea, and enterohemorrhagic *E coli* (EHEC) and *Shigella*, whose toxins cause inflammatory/bloody diarrhea
- Bacterial invasion of the intestinal mucosa by *Salmonella*, enteroinvasive *E coli* (EIEC), and *Campylobacter jejuni* causes inflammatory/bloody diarrhea

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whose toxins cause inflammatory/bloody diarrhea

- Bacterial invasion of the intestinal mucosa by *Salmonella*, enteroinvasive *E coli* (EIEC), and *Campylobacter jejuni* causes inflammatory/bloody diarrhea
- Enteropathogenic *E coli* (EPEC) attaches to enterocytes and effaces their surface, resulting in watery diarrhea; this strain does not produce toxins

However, gastroenteritis due to these bacteria generally takes **>24 hours** to manifest, as the bacteria require time to proliferate and subsequently produce enterotoxin and/or invade the intestinal epithelium.

(Choice E) Most gram-negative enteric pathogens contain endotoxin (lipopolysaccharide) that is released upon cell lysis. However, endotoxin released in the gastrointestinal tract is not typically absorbed in sufficient quantities to cause systemic illness. Endotoxin-mediated illness (eg, sepsis) occurs when gram-negative bacteria are present in the bloodstream.

Educational objective:
Staphylococcal food poisoning is mediated by the ingestion of a preformed, heat-stable enterotoxin that induces rapid-onset (<6 hours) nausea and vomiting. Most cases arise due to improper food handling and storage. Common culprit foods include eggs, dairy products, and mayonnaise-based salads.

Microbiology Infectious Diseases Foodborne illness

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A 30-year-old man is brought to the emergency department due to erratic behavior, progressive right-sided weakness, and difficulty walking for the last month. The patient was diagnosed with HIV several years ago and is not compliant with antiretroviral treatment. Physical examination shows a cachectic and disheveled man. Funduscopic examination shows no abnormalities. Motor strength in the right upper and lower extremities is decreased, and his gait is ataxic. Brain MRI reveals several discrete areas of demyelination in the subcortical and periventricular white matter with no surrounding edema or mass effect. CD4 cell count is 30/mm^3. Reactivation of which of the following pathogens is most likely responsible for this patient's current symptoms?

A. Cytomegalovirus
B. Epstein-Barr virus
C. Herpes simplex virus
D. JC virus
E. Measles virus
F. *Toxoplasma gondii*

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A. ~~Cytomegalovirus~~ (9%)
B. ~~Epstein-Barr virus~~ (2%)
C. ~~Herpes simplex virus~~ (5%)
D. JC virus (73%)
E. Measles virus (1%)
F. ~~*Toxoplasma gondii*~~ (7%)

Correct

73%
Answered correctly

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Last Updated

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Progressive multifocal leukoencephalopathy	
Epidemiology	• JC virus reactivation • Severe immunosuppression (eg, untreated AIDS)
Manifestations	• Slowly progressive • Confusion, paresis, ataxia, seizure
Diagnosis	• MRI of the brain: asymmetric white matter lesions; no enhancement/edema • Lumbar puncture: CSF PCR positive for JC virus • Brain biopsy (rarely needed)
Treatment	• Often fatal • If HIV positive: antiretroviral therapy

CSF = cerebrospinal fluid; **PCR** = polymerase chain reaction.

JC virus is a polyomavirus, typically acquired in childhood, that causes life-long, latent infection of the kidney and lymphoid organs. Most adults have serologic evidence of exposure but remain asymptomatic. However, those with severe immunosuppression, particularly patients with **advanced AIDS**, are at risk for

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JC virus is a polyomavirus, typically acquired in childhood, that causes life-long, latent infection of the kidney and lymphoid organs. Most adults have serologic evidence of exposure but remain asymptomatic. However, those with severe immunosuppression, particularly patients with **advanced AIDS**, are at risk for **viral reactivation** with spread to the brain. The virus attacks **oligodendrocytes**, the cells that produce myelin, causing a severe demyelinating disease called **progressive multifocal leukoencephalopathy** (PML).

PML typically presents with slowly worsening confusion, ataxia, motor deficits, and seizure. Brain MRI usually shows multifocal areas of white matter demyelination with **no mass effect or enhancement**. Diagnosis is confirmed with JC virus PCR testing of the cerebrospinal fluid; brain biopsy is rarely required. There is no specific treatment for PML, but patients with HIV who develop the disease are treated with antiretroviral therapy to reduce immune suppression. This often helps stabilize neurologic symptoms.

(Choice A) Patients with advanced AIDS can occasionally develop cytomegalovirus encephalitis, which usually presents with rapidly progressive altered mental state and focal neurologic deficits. However, this condition is highly inflammatory so brain imaging typically shows enhancing lesions.

(Choice B) Epstein-Barr virus reactivation can cause primary CNS lymphoma in patients with advanced AIDS. Patients usually have focal neurologic symptoms and altered mental state. However, brain MRI normally reveals a single enhancing lesion with mass effect.

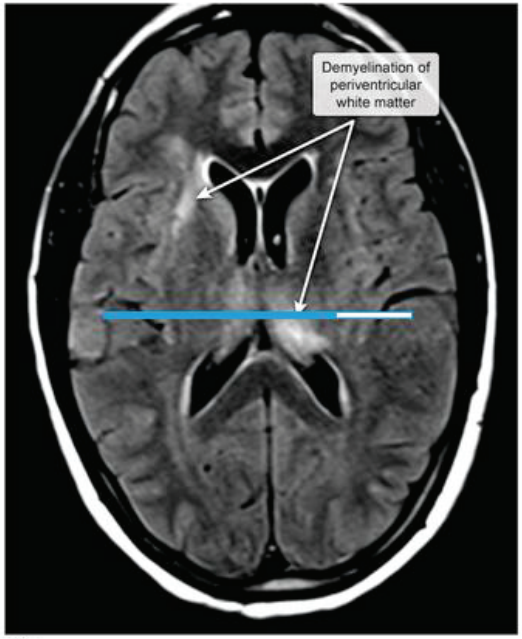
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Exhibit Display

Progressive multifocal leukoencephalopathy



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normally reveals a single enhancing lesion with mass effect

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(Choice B) Epstein-Barr virus reactivation can cause primary CNS lymphoma in patients with advanced AIDS. Patients usually have focal neurologic symptoms and altered mental state. However, brain MRI normally reveals a single enhancing lesion with mass effect.

(Choice C) Herpes simplex virus encephalitis usually causes focal neurologic deficits and altered mental status. However, symptom onset is usually rapid (<1 week), most patients have fever, and brain imaging usually reveals an enhancing temporal lobe lesion with mass effect.

(Choice E) Measles can cause subacute, sclerosing panencephalitis several years after initial infection. This fatal, progressive disease is characterized by slowly worsening neurologic symptoms and multifocal, enhancing, white matter lesions.

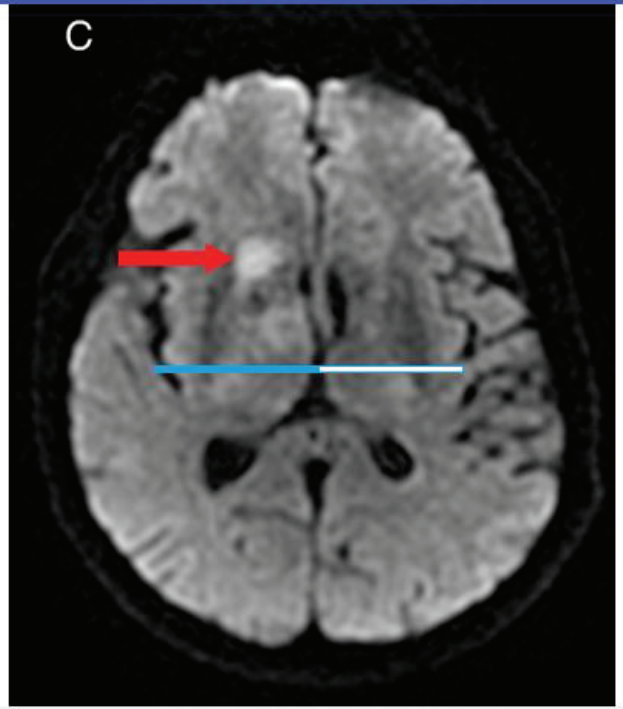
(Choice F) *Toxoplasma gondii* is usually acquired by exposure to cat feces. Most patients are asymptomatic and have a life-long dormant infection. However, patients with advanced AIDS can have reactivation leading to meningoencephalitis (eg, headache, confusion, fever). Brain imaging usually shows several ring-enhancing lesions with surrounding edema.

Educational objective:
Patients with advanced AIDS can have reactivation of JC virus, which causes progressive multifocal leukoencephalopathy. This condition usually presents with slowly progressive confusion, ataxia, and motor

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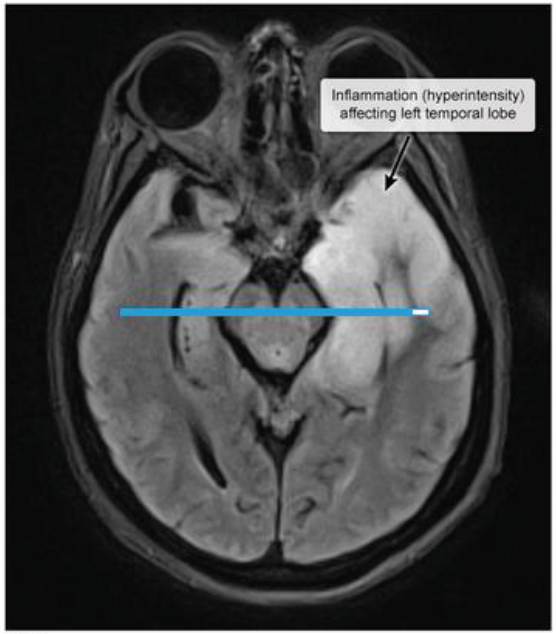
leukoencephalopathy. This condition usually presents with slowly progressive confusion, ataxia, and motor

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Exhibit Display

Herpes encephalitis



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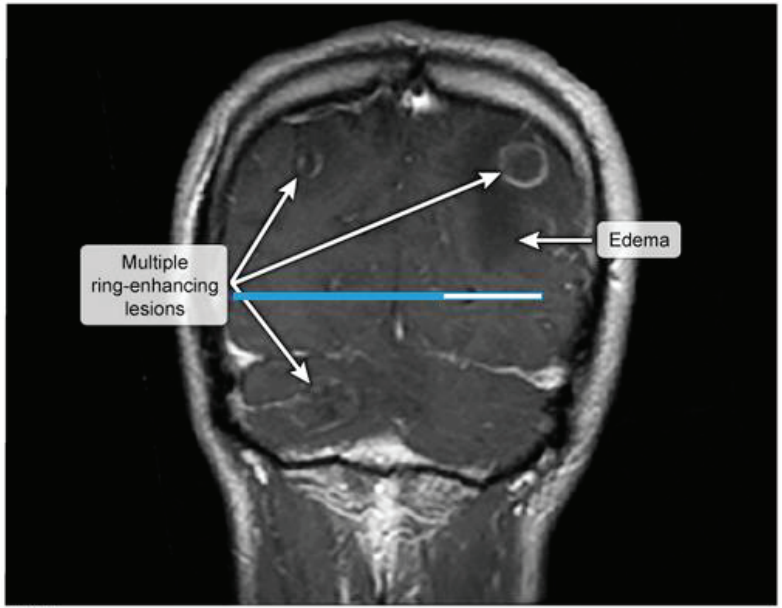
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Toxoplasma encephalitis



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status. However, symptom onset is usually rapid (<1 week), most patients have fever, and brain imaging usually reveals an enhancing temporal lobe lesion with mass effect.

(Choice E) Measles can cause subacute, sclerosing panencephalitis several years after initial infection. This fatal, progressive disease is characterized by slowly worsening neurologic symptoms and multifocal, enhancing, white matter lesions.

(Choice F) *Toxoplasma gondii* is usually acquired by exposure to cat feces. Most patients are asymptomatic and have a life-long dormant infection. However, patients with advanced AIDS can have reactivation leading to meningoencephalitis (eg, headache, confusion, fever). Brain imaging usually shows several ring-enhancing lesions with surrounding edema.

Educational objective:
Patients with advanced AIDS can have reactivation of JC virus, which causes progressive multifocal leukoencephalopathy. This condition usually presents with slowly progressive confusion, ataxia, and motor deficits. Brain MRI reveals multifocal areas of white matter demyelination with no mass effect or enhancement.

Microbiology Infectious Diseases Progressive multifocal leukoencephalopathy

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Several individuals in a Florida neighborhood develop a febrile illness during the summer. Most of them experience abrupt-onset fever, headache, confusion, and lethargy. Some patients also develop tremors, seizures, and focal motor or sensory deficits. Physical examination shows signs of meningeal irritation and altered mental status. Cerebrospinal fluid evaluation reveals lymphocytic pleocytosis with no organisms seen on Gram stain. Brain imaging shows no abnormalities. Which of the following would be most helpful in controlling this disease outbreak?

A. Control of vector arthropods
B. Decontamination of bat droppings
C. Isolation of infected individuals
D. Purification of drinking water
E. Vaccination of all individuals

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Several individuals in a Florida neighborhood develop a febrile illness during the summer. Most of them experience abrupt-onset fever, headache, confusion, and lethargy. Some patients also develop tremors, seizures, and focal motor or sensory deficits. Physical examination shows signs of meningeal irritation and altered mental status. Cerebrospinal fluid evaluation reveals lymphocytic pleocytosis with no organisms seen on Gram stain. Brain imaging shows no abnormalities. Which of the following would be most helpful in controlling this disease outbreak?

- A. Control of vector arthropods (57%)
- B. Decontamination of bat droppings (2%)
- C. Isolation of infected individuals (15%)
- D. Purification of drinking water (14%)
- E. Vaccination of all individuals (9%)

Correct

57%
Answered correctly

01 min, 20 secs
Time Spent

03/05/2021
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Explanation

Common arboviral infections	
Viral pathogens	• West Nile virus • St. Louis encephalitis virus • La Crosse virus • Eastern & Western equine encephalitis viruses
Clinical syndromes	• Most common: asymptomatic to flu-like illness (eg, fever, headache, myalgias) • Meningitis (eg, neck stiffness, headache) • Encephalitis (eg, confusion, tremors, focal neurological deficits) • Acute asymmetric flaccid paralysis: West Nile virus
Transmission	• Arthropod (eg, mosquito, tick) bites • Host: birds and small mammals

These patients have a febrile illness with signs of meningitis (eg, neck stiffness, headache) and

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Transmission	• Host: birds and small mammals

These patients have a febrile illness with signs of meningitis (eg, neck stiffness, headache) and encephalitis (eg, confusion, seizure, tremor, focal deficits), raising strong suspicion for an outbreak of **arbovirus meningoencephalitis** (eg, West Nile virus, La Crosse virus). Arboviruses are small RNA viruses that are harbored by birds and small mammals and are transmitted to humans via biting arthropods (eg, **mosquitos**, ticks, fleas), primarily during the **summer months** when arthropod populations are at their peak.

Infections in otherwise healthy individuals usually result in an asymptomatic low-level viremia that is cleared within a week by the humoral antibody response. In contrast, patients who cannot mount a rapid, effective antibody response (eg, elderly, immunocompromised) may have persistent and more severe viremia; these individuals often develop a severe **flu-like illness** (eg, fever, headache, fatigue, arthralgias) that may progress to **meningitis** and/or **encephalitis**.

Most arbovirus infections are self-limited and resolve with supportive care, but some cases of meningoencephalitis are fatal. Because no vaccines are currently available for North American arboviruses **(Choice E)**, prevention primarily relies on the **elimination of vector arthropod breeding grounds** (eg, stagnant water) and the early identification of infected arthropods (and birds) so that aerosolized insecticide

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meningoencephalitis are fatal. Because no vaccines are currently available for North American arboviruses **(Choice E)**, prevention primarily relies on the **elimination of vector arthropod breeding grounds** (eg, stagnant water) and the early identification of infected arthropods (and birds) so that aerosolized insecticide can be sprayed.

(Choice B) Histoplasmosis is an endemic mycosis of the Ohio and Mississippi River Valleys that can be transmitted by bird or bat droppings. Most patients are asymptomatic, but a minority develop pneumonia. Dissemination to the CNS can occur occasionally but is associated with focal brain lesions on imaging.

(Choice C) Meningococcal meningitis requires isolation of infected individuals (droplet precautions) to prevent transmission. Patients often initially develop flu-like symptoms that can progress within hours to petechial/hemorrhagic rash, sepsis, and death. Cerebrospinal fluid will show neutrophilic pleocytosis.

(Choice D) Aseptic meningitis is often caused by enteroviruses (eg, Coxsackievirus, echovirus) that are transmitted via the fecal-oral route through contaminated food or water. However, enteroviruses are less likely to cause signs of encephalitis (eg, confusion, focal neurologic deficits, tremors, seizures) than arboviruses.

Educational objective:

Arboviruses, small RNA viruses transmitted by biting arthropods, are the most common cause of

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Dissemination to the CNS can occur occasionally but is associated with focal brain lesions on imaging.

(Choice C) Meningococcal meningitis requires isolation of infected individuals (droplet precautions) to prevent transmission. Patients often initially develop flu-like symptoms that can progress within hours to petechial/hemorrhagic rash, sepsis, and death. Cerebrospinal fluid will show neutrophilic pleocytosis.

(Choice D) Aseptic meningitis is often caused by enteroviruses (eg, Coxsackievirus, echovirus) that are transmitted via the fecal-oral route through contaminated food or water. However, enteroviruses are less likely to cause signs of encephalitis (eg, confusion, focal neurologic deficits, tremors, seizures) than arboviruses.

Educational objective:
Arboviruses, small RNA viruses transmitted by biting arthropods, are the most common cause of encephalitis outbreaks in the United States. Because no vaccines are currently available, prevention primarily involves eliminating the vector arthropods (eg, infected mosquitos).

Microbiology	Infectious Diseases	Arbovirus
Subject	System	Topic

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A 23-year-old woman comes to the hospital due to fever, chills, dyspnea, and cough for the past several days. She also has sharp right-sided chest pain exacerbated by breathing. Her temperature is 39 C (102 F), blood pressure is 115/70 mm Hg, and pulse is 108/min. On examination, the patient has several needle track marks on both arms. There is a 3/6 holosystolic murmur heard best at the lower sternal border that increases on inspiration. Chest imaging reveals scattered bilateral peripheral lung opacities. HIV testing is negative. This patient's blood cultures are most likely to grow which of the following organisms?

A. *Candida albicans*
B. *Eikenella corrodens*
C. *Klebsiella pneumoniae*
D. *Nocardia asteroides*
E. *Peptostreptococcus*
F. *Staphylococcus aureus*
G. *Streptococcus gallolyticus* (formerly *S bovis*)
H. *Streptococcus pneumoniae*

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C. *Klebsiella pneumoniae*
D. *Nocardia asteroides*
E. *Peptostreptococcus*
F. *Staphylococcus aureus*
G. *Streptococcus gallolyticus* (formerly *S bovis*)
H. *Streptococcus pneumoniae*
I. *Viridans group streptococcus*

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track marks on both arms. There is a 3/6 holosystolic murmur heard best at the lower sternal border that increases on inspiration. Chest imaging reveals scattered bilateral peripheral lung opacities. HIV testing is negative. This patient's blood cultures are most likely to grow which of the following organisms?

A. *Candida albicans* (1%)
B. *Eikenella corrodens* (0%)
C. *Klebsiella pneumoniae* (1%)
D. *Nocardia asteroides* (0%)
E. *Peptostreptococcus* (0%)
F. *Staphylococcus aureus* (88%)
G. *Streptococcus gallolyticus* (formerly *S bovis*) (0%)
H. *Streptococcus pneumoniae* (1%)
I. *Viridans group streptococcus* (4%)

Incorrect

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***Staphylococcus* aureus** can cause **right-sided endocarditis** in **intravenous drug users** (IVDUs). In patients other than IVDUs, *S aureus* disseminates from a primary disease process (eg, abscess, infected central line) and moves by hematogenous spread to the endocardium. *S aureus* settles on the valve leaflets due to blood flow turbulence at these sites. *S aureus* can cause perforations in the heart valves, rupture the chordae tendineae, and send **septic emboli** to the lung (with right heart endocarditis) or to the brain and systemic circulation (with left heart endocarditis). This patient with fever is an IVDU with a holosystolic murmur that increases with inspiration (likely tricuspid regurgitation) and multiple lung opacities (likely septic emboli). She likely has *S aureus* endocarditis.

(Choice A) *Candida* endocarditis (rare) is typically a severe manifestation of candidemia, with septic emboli to the brain, extremities, and gastrointestinal tract. Patients who are IVDUs, have prosthetic heart valves, or have indwelling lines are at increased risk of infection.

(Choice B) Culture-negative endocarditis - due to *Bartonella, Coxiella, Mycoplasma, Histoplasma, Chlamydia*, or the HACEK organisms (***H**aemophilus, **A**ctinobacillus, **C**ardiobacterium, **E**ikenella*, and ***K**ingella*), among others - would be much less likely than *S aureus* endocarditis.

(Choices C, D, E, and H) *Streptococcus pneumoniae* and *Klebsiella pneumoniae* typically cause

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Kingella), among others - would be much less likely than *S aureus* endocarditis.

(Choices C, D, E, and H) *Streptococcus pneumoniae* and *Klebsiella pneumoniae* typically cause pneumonia; *Klebsiella* can also lead to urinary tract infections. Nocardiosis typically affects the lungs (cavitary lesions), brain (brain abscess), or skin and is seen mostly in immunocompromised patients. *Peptostreptococcus* causes anaerobic infections (dental, cutaneous, intraabdominal).

(Choice G) *Streptococcus gallolyticus* (formerly *S bovis*) is a part of the normal flora of the colon, and bacteremia or endocarditis caused by *S bovis* is associated with colon cancer (~25% of cases).

(Choice I) *Streptococcus viridans* is the most common etiologic agent in subacute bacterial endocarditis (SBE) following dental work. SBE occurs most frequently in patients with a preexisting valvular abnormality (eg, rheumatic heart disease, congenital heart malformations). The presentation is typically subacute (over weeks rather than days).

Educational objective:

Staphylococcus aureus causes acute bacterial endocarditis with rapid onset of symptoms, including shaking chills (rigors), high fever, dyspnea on exertion, and malaise. In intravenous drug users, it can cause right-sided endocarditis with septic embolization into the lungs.

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A 32-year-old man comes to the office due to diarrhea, flatulence, foul-smelling stools, and abdominal cramping. He recently returned home from a hiking trip. A smear of his stool sample is shown below:

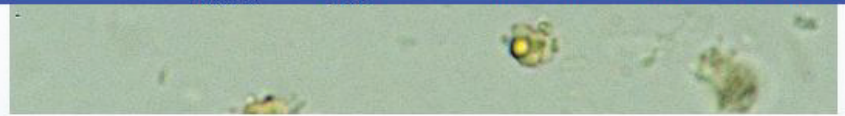


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Which of the following is the drug of choice for this condition?

A. Ciprofloxacin

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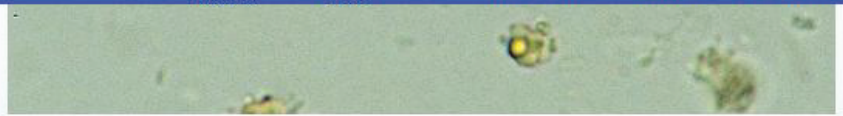
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Which of the following is the drug of choice for this condition?

- A. Ciprofloxacin
- B. Metronidazole
- C. Mebendazole
- D. Albendazole
- E. Loperamide
- F. Clindamycin
- G. Erythromycin

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Which of the following is the drug of choice for this condition?

- A. Ciprofloxacin (2%)
- ✓ B. Metronidazole (79%)
- C. Mebendazole (9%)
- D. Albendazole (4%)
- E. Loperamide (1%)
- F. Clindamycin (1%)
- G. Erythromycin (0%)

Correct

79%

42 secs

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When examined for ova and parasites (stool smear with iodine staining), this patient's stool reveals ellipsoidal cysts with smooth, well-defined walls and 2+ nuclei, consistent with ***Giardia lamblia***. Other classic findings include pear-shaped, flagellated trophozoites. Giardia is the most common enteric parasite in the United States and Canada. When an individual drinks **contaminated water** from an endemic area without first boiling it, *Giardia* can colonize the duodenal and jejunal mucosal lining. Hikers and campers are particularly susceptible to infection.

Giardiasis causes chronic **diarrhea**, malabsorption, and **flatulence**. **Metronidazole** is an accepted treatment for this protozoan flagellate. This drug can also be used to treat *Helicobacter pylori* infections, amebiasis, and trichomoniasis.

(Choice A) Inflammatory traveler's diarrhea (marked by stool containing blood and mucus) can be treated with ciprofloxacin or another fluoroquinolone. Cysts would not be present.

(Choice C) Mebendazole is an anti-helminthic drug that acts on the microtubules of roundworms such as *Ancylostoma*, *Ascaris*, and *Enterobius*.

(Choice D) Albendazole is used to treat the tapeworm (cestode) *Echinococcus granulosus*. Echinococcus does not commonly cause diarrhea, but rather produces cysts in the liver and elsewhere.

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(Choice D) Albendazole is used to treat the tapeworm (cestode) *Echinococcus granulosus.* Echinococcus does not commonly cause diarrhea, but rather produces cysts in the liver and elsewhere.

(Choice E) Loperamide is an opiate antimotility drug that may be prescribed in some cases of traveler's diarrhea where there is no fever or blood in the stool.

(Choice F) Clindamycin has activity against anaerobes (eg, *Bacteroides fragilis*) and has some activity against some strains of staphylocci and streptococci.

(Choice G) Erythromycin can be used in lieu of fluoroquinolones to treat *Campylobacter jejuni*, as this organism has shown increasing worldwide resistance to fluoroquinolones.

Educational objective:

Giardia lamblia is the most common enteric parasite in the United States and Canada and is a common cause of diarrhea in campers/hikers. Iodine-stained stool smear classically shows pear-shaped, flagellated trophozoites or ellipsoidal cysts with smooth, well-defined walls and 2+ nuclei. Metronidazole is the treatment of choice.

Microbiology	Infectious Diseases	Giardia
Subject	System	Topic

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A 28-year-old woman is brought to the emergency department due to abrupt onset of high fever, severe headache, photophobia, and confusion. Temperature is 38.9 C (102 F), blood pressure is 90/60 mm Hg, and pulse is 118/min. On examination, the patient is obtunded and diaphoretic. There is increased resistance to passive neck flexion. Pupillary reflexes are brisk and symmetric, and the patient moves all extremities equally to painful stimuli. Lumbar puncture is performed, and cerebrospinal fluid (CSF) analysis reveals neutrophilic pleocytosis, elevated protein, and low glucose. CSF Gram stain shows no bacteria, and fungal antigen testing is negative. Wet mount preparation of the CSF shows motile trophozoites. Which of the following most likely predisposed this patient to her current condition?

A. Cohabitation with a person with a similar illness
B. Hiking in wooded areas of New England
C. Participation in recreational water activities
D. Recent business trip to Southeast Asia
E. Unprotected intercourse with a new partner

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headache, photophobia, and confusion. Temperature is 38.9 C (102 F), blood pressure is 90/60 mm Hg, and pulse is 118/min. On examination, the patient is obtunded and diaphoretic. There is increased resistance to passive neck flexion. Pupillary reflexes are brisk and symmetric, and the patient moves all extremities equally to painful stimuli. Lumbar puncture is performed, and cerebrospinal fluid (CSF) analysis reveals neutrophilic pleocytosis, elevated protein, and low glucose. CSF Gram stain shows no bacteria, and fungal antigen testing is negative. Wet mount preparation of the CSF shows motile trophozoites. Which of the following most likely predisposed this patient to her current condition?

A. Cohabitation with a person with a similar illness (3%)
B. Hiking in wooded areas of New England (6%)
✓ C. Participation in recreational water activities (63%)
D. Recent business trip to Southeast Asia (15%)
E. Unprotected intercourse with a new partner (11%)

Correct

63%

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Primary amoebic encephalitis	
Pathophysiology	• Infection with ***Naegleria fowleri*** (free-living, motile protozoan) • Exposure during **recreational water activities** (eg, boating, diving) • Mucosal invasion → penetration of cribriform plate → meningoencephalitis
Presentation	• Acute fever, confusion, headache, photophobia, CN palsies • CSF - ↑ protein, neutrophils; **motile trophozoites** on wet mount
Management	• Nearly all cases are **fatal** • Antibiotics (eg, amphotericin B) administered but usually insufficient

CN = cranial nerve; **CSF** = cerebrospinal fluid.

This patient has meningeal signs, confusion, and trophozoites in her cerebrospinal fluid (CSF), raising strong suspicion for **primary amebic meningoencephalitis** (PAM). PAM is caused by ***Naegleria fowleri***, a free-living, motile, protozoan parasite that lives in warm water and soil worldwide. Exposure primarily occurs when humans inadvertently inhale the organism during **recreational water activities** such as swimming, diving, or using hot springs. Most individuals do not become ill, but a minority develop fatal

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meningoencephalitis after *N fowleri* penetrates the olfactory mucosa, crosses the cribriform plate, and invades the olfactory bulb.

Patients with PAM usually develop acute confusion, high fever, photophobia, and meningeal symptoms (eg, neck stiffness, headache). Lumbar puncture opening pressures are often markedly elevated, and CSF analysis typically reveals neutrophilic pleocytosis, high protein, and low glucose. Suspicion is usually raised when CSF testing is negative for bacterial, viral, or fungal pathogens. The diagnosis is confirmed when **wet mount** of the CSF reveals **motile trophozoites**. Antibiotics (eg, amphotericin B) are often administered, but PAM is almost always fatal.

(Choice A) *Neisseria meningitidis* is a gram-negative bacterium that is typically spread by close contact with a carrier or infected individual. It is a common cause of community-acquired bacterial meningitis and usually presents with rapidly progressive headache, myalgia, confusion, sepsis, and death. Patients also frequently have an ecchymotic/purpuric rash. Diagnosis is often made with blood culture and/or CSF Gram stain.

(Choice B) Lyme disease, a tick-borne illness caused by the spirochete *Borrelia burgdorferi*, is endemic to the wooded areas of New England. Patients with early disseminated Lyme disease can sometimes develop cranial nerve palsies or lymphocytic meningitis, but wet mount of the CSF would not show

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(Choice B) Lyme disease, a tick-borne illness caused by the spirochete *Borrelia burgdorferi*, is endemic to the wooded areas of New England. Patients with early disseminated Lyme disease can sometimes develop cranial nerve palsies or lymphocytic meningitis, but wet mount of the CSF would not show trophozoites. Diagnosis of early disseminated Lyme disease is usually made with serology.

(Choice D) Malaria is a mosquito-borne protozoal illness that is endemic to Southeast Asia. Patients with malaria can develop encephalopathy (cerebral malaria) with confusion, headache, and delirium. However, CSF analysis is usually fairly normal, and trophozoites are not typically seen in the CSF. Malaria is usually diagnosed when trophozoites are isolated on peripheral blood smear.

(Choice E) Syphilis is caused by the spirochete *Treponema pallidium* and is transmitted primarily by unprotected sexual intercourse. Patients with syphilis infections can occasionally develop lymphocytic meningitis early in infection. However, syphilis is usually diagnosed with serology; trophozoites would not be present in the CSF.

Educational objective:

Naegleria fowleri is a free-living, motile protozoan that lives in warm water. Exposure can result in primary amebic encephalitis, which is characterized by acute fever, headache, confusion, and neck stiffness. The diagnosis is confirmed when motile trophozoites are seen on cerebrospinal fluid wet mount. Nearly all patients die

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An 8-year-old boy who recently moved to the United States from Indonesia is brought to the emergency department due to fever, sore throat, and difficulty breathing. His immunization status cannot be determined. Physical examination shows extensive, coalescing, gray pharyngeal exudate and cervical adenopathy. Several days after being admitted to the hospital, he dies of myocarditis and severe heart failure. The presence of which of the following would most likely have prevented this patient's death?

A. Activated CD8 T lymphocytes
B. Complement-fixing IgM
C. IgA against capsular proteins
D. IgG against circulating proteins
E. IgM from T-cell–independent response

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An 8-year-old boy who recently moved to the United States from Indonesia is brought to the emergency department due to fever, sore throat, and difficulty breathing. His immunization status cannot be determined. Physical examination shows extensive, coalescing, gray pharyngeal exudate and cervical adenopathy. Several days after being admitted to the hospital, he dies of myocarditis and severe heart failure. The presence of which of the following would most likely have prevented this patient's death?

A. Activated CD8 T lymphocytes (8%)
B. Complement-fixing IgM (5%)
C. IgA against capsular proteins (12%)
✓ D. IgG against circulating proteins (68%)
E. IgM from T-cell–independent response (5%)

Correct

68%
Answered correctly

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Diphtheria	
Epidemiology	• Rare in developed countries due to widespread vaccination • Risk: inadequate vaccination/10-year booster shot
Pathogenesis	• **Toxigenic *Corynebacterium diphtheriae*** colonizes respiratory tract → secretes **diphtheria toxin** → inhibits host protein synthesis (ADP-ribosylation of EF-2) → local and systemic toxin-mediated effects
Manifestations	• Local: **pseudomembranous pharyngitis**, cervical LAD • Systemic: **myocarditis**/heart failure, neurologic toxicity • Pharyngeal edema/pseudomembrane spread can obstruct respiratory tract
Treatment	• **Diphtheria antitoxin** (most important) • Antibiotics

EF-2 = elongation factor-2; **LAD** = lymphadenopathy.

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EF-2 = elongation factor-2; **LAD** = lymphadenopathy.

This patient with an uncertain vaccination history likely died from **diphtheria**, a clinical illness caused by **toxigenic strains** of *Corynebacterium diphtheriae*. The disease is rare in the developed world due to widespread vaccination with diphtheria toxoid, but outbreaks often occur in regions where vaccination efforts are insufficient (eg, Southeast Asia). Most cases are transmitted by aerosolized droplets from asymptomatic carriers or infected patients. Although the pathogen has little capacity for invasion, it generates a **potent exotoxin** (diphtheria toxin) that irreversibly inhibits protein synthesis through ADP-ribosylation of elongation factor-2, leading to host cell death and necrosis. Local effects of the toxin include pharyngitis and laryngotracheitis, often with an **extensive**, **coalescing exudate** (pseudomembrane). Absorption of the toxin into the bloodstream results in potentially life-threatening **myocarditis** and neuritis.

Diphtheria can be prevented with the diphtheria-pertussis-tetanus (DPT) childhood vaccination, which generates **neutralizing IgG antibodies** against the binding component (B subunit) of the diphtheria exotoxin. The vaccine inhibits toxin-mediated cell damage and also reduces the competitive advantage of toxigenic strains, thereby reducing toxigenic carriage rates within the population.

(Choice A) CD8 lymphocytes destroy cells infected with intracellular pathogens (eg, viruses) as well as cells damaged by cancer. They do not bind to and eliminate circulating exotoxins.

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(Choice A) CD8 lymphocytes destroy cells infected with intracellular pathogens (eg, viruses) as well as cells damaged by cancer. They do not bind to and eliminate circulating exotoxins.

(Choices B and E) IgM opsonization and complement fixation are important mechanisms for combating extracellular infections, particularly with encapsulated organisms. Although vaccination may stimulate an IgM response, long-term protection is primarily mediated by IgG antibodies.

(Choice C) IgA is the primary immunoglobulin found on mucosal surfaces and in secretions. It does not have significant opsonizing or complement-activating properties. Instead, it prevents infection by inhibiting bacterial interaction with epithelial cells (eg, attachment, invasion). IgA antibodies may help prevent diphtheria colonization. However, *C diphtheriae* does not have a polysaccharide capsule.

Educational objective:
Toxigenic strains of *Corynebacterium diphtheriae* produce diphtheria toxin, which irreversibly inhibits host protein synthesis due to ADP-ribosylation of elongation factor-2. Local effects include pseudomembranous pharyngitis; systemic effects include potentially life-threatening myocarditis and neuritis. Immunization with diphtheria toxoid generates protective circulating IgG against the exotoxin B subunit.

Microbiology Infectious Diseases Diphtheria

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A 31-year-old man comes to the office due to a week of fever, night sweats, sore throat, malaise, and extreme fatigue. He has no prior medical conditions and takes no medications. The patient has had multiple sexual partners over his lifetime and uses condoms inconsistently. Temperature is 38 C (100.4 F), blood pressure is 110/80 mm Hg, pulse is 92/min, and respirations are 20/min. Physical examination shows multiple shallow ulcers on the oropharyngeal mucosa, and the tonsils are enlarged and hyperemic. Cervical and axillary lymphadenopathy is present, and there is a generalized, erythematous, maculopapular skin rash. HIV testing shows the following results:

Anti-HIV antibodies	negative
HIV p24 antigen	positive
Plasma HIV RNA	detectable

Which of the following best explains this patient's laboratory findings?

A. Early viral infection before serologic response

B. High antigenic variability of the surface glycoprotein

C. Inadequate antibody production due to immunosuppression

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Cervical and axillary lymphadenopathy is present, and there is a generalized, erythematous, maculopapular skin rash. HIV testing shows the following results:

Anti-HIV antibodies	negative
HIV p24 antigen	positive
Plasma HIV RNA	detectable

Which of the following best explains this patient's laboratory findings?

A. Early viral infection before serologic response
B. High antigenic variability of the surface glycoprotein
C. Inadequate antibody production due to immunosuppression
D. Insufficient viral replication necessary for antibody production
E. Underlying primary immunodeficiency

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Cervical and axillary lymphadenopathy is present, and there is a generalized, erythematous, maculopapular skin rash. HIV testing shows the following results:

Anti-HIV antibodies	negative
HIV p24 antigen	positive
Plasma HIV RNA	detectable

Which of the following best explains this patient's laboratory findings?

- A. Early viral infection before serologic response (71%)
- B. High antigenic variability of the surface glycoprotein (6%)
- C. Inadequate antibody production due to immunosuppression (13%)
- D. Insufficient viral replication necessary for antibody production (3%)
- E. Underlying primary immunodeficiency (4%)

Correct

71%
Answered correctly

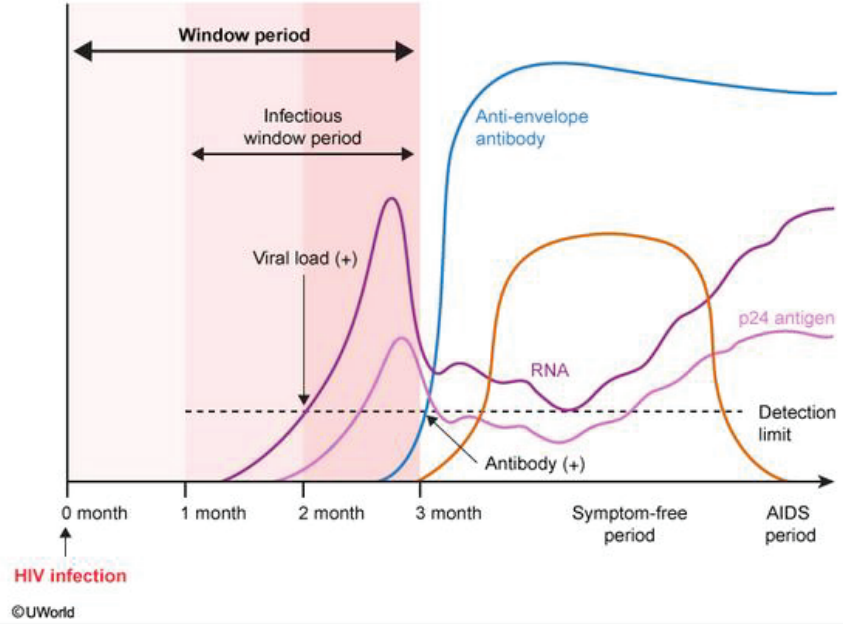
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HIV antibody testing



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Most patients infected with **HIV** develop mononucleosis-like symptoms (eg, fever, diffuse lymphadenopathy, malaise, myalgia, sore throat, and headache) 2-4 weeks after inoculation (**acute retroviral syndrome**). The presence of **oropharyngeal ulcers** and a diffuse **maculopapular rash** are important diagnostic clues.

Acute retroviral syndrome is associated with extremely **high levels of viral replication** (~5 million copies/mL) as the cell-mediated and humoral antibody response against the virus is not yet fully activated. Therefore, laboratory results during this period usually show evidence of HIV in the plasma (positive viral load and p24 antigen) with a **negative serologic response** (negative HIV-1/HIV-2 antibody). This is referred to as the **"window period,"** as patients are infected with HIV but HIV antibody screening tests may be negative (newer screening tests incorporate testing for HIV p24 antigen and are more sensitive in early infection).

The humoral response to HIV typically develops 6-8 weeks after initial infection. At this time, anti-HIV antibodies in the serum neutralize circulating virus, which reduces viral load and leads to resolution of acute retroviral symptoms. Most patients then enter a long asymptomatic period until diminished CD4 counts open the door to opportunistic infections.

(Choice B) Antibodies against HIV surface glycoproteins (eg, gp120) help neutralize circulating virus and reduce viral load. However, HIV surface glycoproteins display a high degree of antigenic variation, which

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(Choice B) Antibodies against HIV surface glycoproteins (eg, gp120) help neutralize circulating virus and reduce viral load. However, HIV surface glycoproteins display a high degree of antigenic variation, which prevents the formation of a completely effective antibody response.

(Choices C and E) Patients with HIV develop immunosuppression primarily due to impairments in the cell-mediated immune response. Although the humoral immune response is also impaired, patients are able to generate anti-HIV antibodies that partially neutralize the virus. It is very rare that a patient with HIV will be too immunodeficient to seroconvert.

(Choice D) Acute retroviral syndrome is marked by an extremely high rate of viral replication. Although antibodies eventually form, the response is delayed because the humoral immune response takes several weeks to fully develop.

Educational objective:
Initial HIV infection is often associated with mononucleosis-like symptoms (eg, fever, lymphadenopathy, sore throat) 2-4 weeks after transmission. Important diagnostic clues are oropharyngeal ulcers and a diffuse maculopapular rash. As the humoral antibody response is not fully activated early in infection, laboratory results typically show HIV in the serum (positive viral load and p24 antigen) but negative HIV serology

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A 32-year-old man comes to the office due to 2 weeks of fever, malaise, and arthralgia. Temperature is 38.2 C (100.8 F) and pulse is 102/min. Physical examination reveals several enlarged cervical, axillary, and inguinal lymph nodes and a diffuse maculopapular skin rash. Serum aminotransferase levels are elevated. During further testing, the patient's serum is added to a mixture of cardiolipin, cholesterol, and lecithin, which leads to extensive clumping and flocculation. Evaluation for antibodies directed against which of the following is the best next step in management of this patient?

A. *Borrelia burgdorferi*

B. Fc portion of IgG

C. *Histoplasma capsulatum*

D. Mitochondrial components

E. *Treponema pallidum*

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A. *Borrelia burgdorferi* (13%)
B. Fc portion of IgG (16%)
C. *Histoplasma capsulatum* (4%)
D. Mitochondrial components (8%)
✓ E. *Treponema pallidum* (56%)

Correct

56%
Answered correctly

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Syphilis: diagnostic serology	
Nontreponemal (RPR, VDRL)	• Antibody to **cardiolipin-cholesterol-lecithin antigen** • Lower sensitivity in early infection
Treponemal (FTA-ABS, TP-EIA)	• Antibody to **treponemal antigens** • Greater sensitivity in early infection

FTA-ABS = fluorescent treponemal antibody-absorption (test); **RPR** = rapid plasma reagin (test);
TP-EIA = *Treponema pallidum* enzyme immunoassay.

This patient has fever, arthralgias, diffuse lymphadenopathy, elevated aminotransferases, and widespread maculopapular rash raising suspicion for secondary syphilis. Syphilis is a multistage infection caused by the spirochete ***Treponema pallidum***. Diagnostic screening and confirmation rely primarily on serologic testing.

Nontreponemal serologic tests (rapid plasma reagin, VDRL) mix a patient's serum with a cardiolipin-cholesterol-lecithin antigen. Aggregation or flocculation (clumping) indicates the presence of **anticardiolipin antibodies** in the patient's serum. These antibodies form in response to the release of lipids from cells damaged by *T pallidum*. However, anticardiolipin antibodies are **nonspecific**; they can

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Syphilis manifestations	
Primary	• Painless genital ulcer (chancre)
Secondary	• Diffuse rash (palms & soles) • Lymphadenopathy (epitrochlear) • Condyloma latum • Oral lesions • Hepatitis
Latent	• Asymptomatic
Tertiary	• CNS (tabes dorsalis, dementia) • Cardiovascular (aortic aneurysm/insufficiency) • Cutaneous (gummas)

CNS = central nervous system.

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lipids from cells damaged by *T pallidum*. However, anticardiolipin antibodies are **nonspecific**; they can also develop in other treponemal (eg, yaws, pinta, bejel) and nontreponemal (eg, tuberculosis) infections and certain rheumatologic diseases (eg, lupus), which can lead to false-positive results.

Positive nontreponemal screening requires diagnostic confirmation with **treponemal serologic testing** (eg, fluorescent treponemal antibody-absorption). Treponemal tests evaluate for **antibodies that directly target *T pallidum***; patient serum is mixed with killed *T pallidum* to evaluate for antibody adherence using immunofluorescence. Patients with positive nontreponemal and treponemal tests are considered infected with syphilis.

(Choice A) Lyme disease is caused by the spirochete *Borrelia burgdorferi*. Patients with early Lyme disease often develop flulike symptoms and a bull's-eye rash (not a diffuse maculopapular rash). Serologic testing for IgM/IgG against *Borrelia* can aid in the diagnosis as the disease progresses.

(Choice B) Rheumatoid factor is an antibody that targets the Fc portion of IgG. Elevations are often seen in patients with rheumatoid arthritis and other autoimmune diseases.

(Choice C) *Histoplasma capsulatum* infection can be diagnosed by examining urine and serum for fungal antigens. *Histoplasma* infections usually present with prominent pulmonary manifestations rather than diffuse rash and lymphadenopathy.

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in patients with rheumatoid arthritis and other autoimmune diseases.

(Choice C) *Histoplasma capsulatum* infection can be diagnosed by examining urine and serum for fungal antigens. *Histoplasma* infections usually present with prominent pulmonary manifestations rather than diffuse rash and lymphadenopathy.

(Choice D) Antimitochondrial antibodies are present in >95% of cases of primary biliary cholangitis, which usually causes fatigue, pruritus, hepatomegaly, and elevated alkaline phosphatase. This patient's systemic maculopapular rash and diffuse lymphadenopathy make syphilis more likely.

Educational objective:

Syphilis is caused by the spirochete *Treponema pallidum*. Confirmation of the diagnosis requires 2 forms of serologic testing to prevent false-positive results. Nontreponemal tests (eg, rapid plasma reagin, VDRL) evaluate for anticardiolipin antibodies (nonspecific); treponemal tests evaluate for antibodies targeted against *T pallidum*.

Microbiology	Infectious Diseases	Syphilis
Subject	System	Topic

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A 25-year-old primigravida has a stillbirth at 18 weeks gestation. Her only symptom during pregnancy was pain in both knees and feet, which she attributed to pregnancy-related weight gain and being "on my feet all day" as an elementary school teacher. The pain lasted approximately a week and resolved without medication. The patient was taking prenatal vitamins daily, and her prenatal care was appropriate. Fetal autopsy shows pleural effusion, pulmonary hypoplasia, and ascites. Infection with which of the following is the most likely etiology of the stillbirth?

A. Enveloped, double-stranded DNA virus
B. Enveloped, single-stranded RNA virus
C. Gram-positive coccus in chains
D. Nonenveloped, single-stranded DNA virus
E. Obligate intracellular protozoa

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A 25-year-old primigravida has a stillbirth at 18 weeks gestation. Her only symptom during pregnancy was pain in both knees and feet, which she attributed to pregnancy-related weight gain and being "on my feet all day" as an elementary school teacher. The pain lasted approximately a week and resolved without medication. The patient was taking prenatal vitamins daily, and her prenatal care was appropriate. Fetal autopsy shows pleural effusion, pulmonary hypoplasia, and ascites. Infection with which of the following is the most likely etiology of the stillbirth?

A. Enveloped, double-stranded DNA virus (20%)
B. Enveloped, single-stranded RNA virus (22%)
C. Gram-positive coccus in chains (6%)
✓ D. Nonenveloped, single-stranded DNA virus (46%)
E. Obligate intracellular protozoa (4%)

Correct

46%
Answered correctly

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Parvovirus is a nonenveloped **single-stranded (ss) DNA virus** with an increased incidence in children and teachers, as most individuals are infected during **school outbreaks**. Infection in adults can present with an acute, symmetric **arthralgia/arthritis** involving hands, wrists, knees, and/or feet, with or without rash.

Fetal infection with parvovirus can lead to **interruption of erythropoiesis**, causing **profound anemia** and congestive heart failure. Fetal congestive heart failure can cause pleural effusions, pericardial effusions, and **ascites**. The findings on fetal autopsy (pleural effusion with secondary pulmonary hypoplasia, and ascites) represent **fetal hydrops**.

Parvovirus is also responsible for erythema infectiosum ("fifth disease"), which presents with a "slapped cheek" appearance in children, and aplastic crisis in patients with sickle cell anemia.

(Choice A) Varicella zoster virus (VZV) and cytomegalovirus (CMV) are examples of enveloped, double-stranded DNA viruses. VZV exposure in the second trimester increases the risk of fetal varicella syndrome (presents as limb hypoplasia, microcephaly, chorioretinitis). Congenital CMV can cause jaundice, hepatosplenomegaly, and periventricular calcifications. Congenital CMV (and other TORCH infections), when severe, can also cause hydrops due to multiorgan failure. However, parvovirus is the most common infectious agent causing hydrops and is especially likely given the mother's history of transient arthralgias during pregnancy.

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Congenital TORCH infections

Organism	Etiology	Clinical features
Toxoplasmosis	Obligate intracellular protozoan *Toxoplasma gondii*	Chorioretinitis, intracranial calcifications, hydrocephalus
Other (VZV, parvovirus)	• VZV: dsDNA virus • Parvovirus: ssDNA virus • Syphilis: spirochete *Treponema pallidum*	• VZV: limb hypoplasia, cutaneous scarring, cataracts, chorioretinitis • Parvovirus: hydrops fetalis • Syphilis: "snuffles," hepatomegaly, skeletal anomalies
Rubella	ssRNA virus	Sensorineural deafness, cataracts, "blueberry muffin" rash, heart defects, hepatosplenomegaly
CMV	dsDNA virus	Sensorineural deafness, periventricular calcifications, jaundice, hepatosplenomegaly, chorioretinitis
HSV	dsDNA virus	Cutaneous vesicles, lesions, scarring

CMV = cytomegalovirus; **ds** = double-stranded; **HSV** = herpes simplex virus; **ss** = single-stranded; **VZV** = varicella zoster

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during pregnancy.

(Choice B) Rubella is an enveloped ssRNA virus. Congenital rubella infection characteristically causes cataracts, sensorineural deafness, and a "blueberry muffin" rash (purpuric lesions signify dermal erythropoiesis).

(Choice C) Group B streptococcus (GBS) is a gram-positive coccus that is present in chains and colonizes the female genital and gastrointestinal tracts. Fetuses exposed to GBS via the amniotic fluid during labor, or with rupture of membranes, can develop sepsis a few days after birth. GBS exposure does not cause hydrops fetalis.

(Choice E) Congenital toxoplasmosis leads to chorioretinitis, hydrocephalus, intracranial calcifications, microcephaly, and seizures. It is caused by an obligate intracellular protozoan, *Toxoplasma gondii*.

Educational objective:
Infection with parvovirus B19 (a nonenveloped single-stranded DNA virus) can cause arthralgia with or without rash in adults. An infected fetus may develop hydrops fetalis (severe anemia, heart failure, pleural effusions, pericardial effusions, and ascites).

References

- Parvovirus B19 during pregnancy: a review.

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A 12-year-old boy is brought to the emergency department by paramedics after being found unresponsive at home. He had 24 hours of headache, nausea, and fever, which his parents were treating with acetaminophen. His temperature is 39.6 C (103.4 F). Physical examination reveals neck stiffness. Lumbar puncture is performed. Analysis of cerebrospinal fluid shows marked pleocytosis, and Gram stain shows gram-negative cocci in pairs. The parents are concerned about their younger son, who shares a bedroom with the patient. Which of the following is the most appropriate management of this patient's household contacts?

A. Immediate vaccination
B. Observation only
C. Prophylactic penicillin
D. Prophylactic rifampin
E. Prophylactic sulfamethoxazole

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A 12-year-old boy is brought to the emergency department by paramedics after being found unresponsive at home. He had 24 hours of headache, nausea, and fever, which his parents were treating with acetaminophen. His temperature is 39.6 C (103.4 F). Physical examination reveals neck stiffness. Lumbar puncture is performed. Analysis of cerebrospinal fluid shows marked pleocytosis, and Gram stain shows gram-negative cocci in pairs. The parents are concerned about their younger son, who shares a bedroom with the patient. Which of the following is the most appropriate management of this patient's household contacts?

A. Immediate vaccination (7%)
B. Observation only (4%)
C. Prophylactic penicillin (8%)
✓ D. Prophylactic rifampin (76%)
E. Prophylactic sulfamethoxazole (3%)

76% 57 secs 02/26/2021

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This patient's presentation and the finding of gram-negative diplococci highly suggest meningitis due to ***Neisseria meningitidis***. *N meningitidis* is transmitted by direct contact with contaminated **respiratory secretions** or aerosolized droplets. As a result, people with **close** or **intimate** contact (eg, household contacts, kissing contacts, health care workers who directly contacted secretions) are at markedly increased risk of meningococcal infection. **Antibiotic** chemoprophylaxis can prevent these secondary cases if given promptly. A history of meningococcal vaccination does not preclude the need for antibiotic chemoprophylaxis.

Of the listed agents, **rifampin** is the only effective choice. Rifampin penetrates well into all body compartments, including the upper respiratory tract, and will eliminate nasopharyngeal colonization. Other effective agents include ciprofloxacin (not routinely used in children due to concerns about connective tissue injury) and intramuscular ceftriaxone, which is effective but not widely used due to the painful mode of administration. Chemoprophylaxis should be given as soon as possible, preferably within 24 hours of diagnosis.

(Choice A) Vaccination is an important public health strategy for control of meningococcal disease in general, but does not play a role in post-exposure prophylaxis. Immunity following a post-exposure vaccination does not occur in time to prevent disease.

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(Choice A) Vaccination is an important public health strategy for control of meningococcal disease in general, but does not play a role in post-exposure prophylaxis. Immunity following a post-exposure vaccination does not occur in time to prevent disease.

(Choice B) A person's risk for infection is 500-1,000 times greater following an exposure to a meningococcal disease patient, and disease onset can be rapid. Therefore, observation alone is not an appropriate strategy for exposed close contacts.

(Choice C) Although penicillin can be used for treatment of susceptible meningococcal infections, it has not been shown to eliminate nasal carriage or prevent secondary cases. Therefore, it should not be used for chemoprophylaxis.

(Choice E) Sulfamethoxazole was the first agent to be used as chemoprophylaxis for meningococcal disease. However, it is no longer an effective agent due to widespread resistance.

Educational objective:
Rifampin is the most frequently used agent for chemoprophylaxis of meningococcal disease. Persons with exposure to the respiratory secretions of a patient with meningococcal disease require chemoprophylaxis. Vaccination is an important public health strategy but is not useful for post-exposure prophylaxis.

References

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A neonate is born at 38 weeks gestation age via spontaneous vaginal delivery to a 40-year-old woman. The mother was working in South America when she discovered that she was pregnant. She had 2 days of fever associated with cough and swollen cervical glands, which resolved spontaneously at 12 weeks gestation prior to returning to the United States. The mother has no current symptoms. Neonatal examination shows weight and length at the 8th percentile, and head circumference below the 3rd percentile for age. Heart and lung sounds are normal. There is moderate hepatosplenomegaly. Skin examination shows diffuse, dark-blue papules and nodules. Serology from the mother and infant are attained. Which of the following serology patterns is most consistent with a suspected congenital infection?

	IgM levels in the mother	IgG levels in the mother	IgM levels in the newborn	IgG levels in the newborn
A.	↑	–	↑	–
B.	–	↑	↑	↑
C.	↑	↑	–	–

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gestation prior to returning to the United States. The mother has no current symptoms. Neonatal examination shows weight and length at the 8th percentile, and head circumference below the 3rd percentile for age. Heart and lung sounds are normal. There is moderate hepatosplenomegaly. Skin examination shows diffuse, dark-blue papules and nodules. Serology from the mother and infant are attained. Which of the following serology patterns is most consistent with a suspected congenital infection?

	IgM levels in the mother	IgG levels in the mother	IgM levels in the newborn	IgG levels in the newborn
A.	↑	–	↑	–
B.	–	↑	↑	↑
C.	↑	↑	–	–
D.	↑	–	–	↑

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gestation prior to returning to the United States. The mother has no current symptoms. Neonatal examination shows weight and length at the 8th percentile, and head circumference below the 3rd percentile for age. Heart and lung sounds are normal. There is moderate hepatosplenomegaly. Skin examination shows diffuse, dark-blue papules and nodules. Serology from the mother and infant are attained. Which of the following serology patterns is most consistent with a suspected congenital infection?

	IgM levels in the mother	IgG levels in the mother	IgM levels in the newborn	IgG levels in the newborn	
A.	↕	=	↕	=	(0%)
✓ B.	=	↕	↕	↕	(100%)
C.	↑	↑	–	–	(0%)
✗ D.	↑	–	–	↑	(0%)

Incorrect
Correct answer

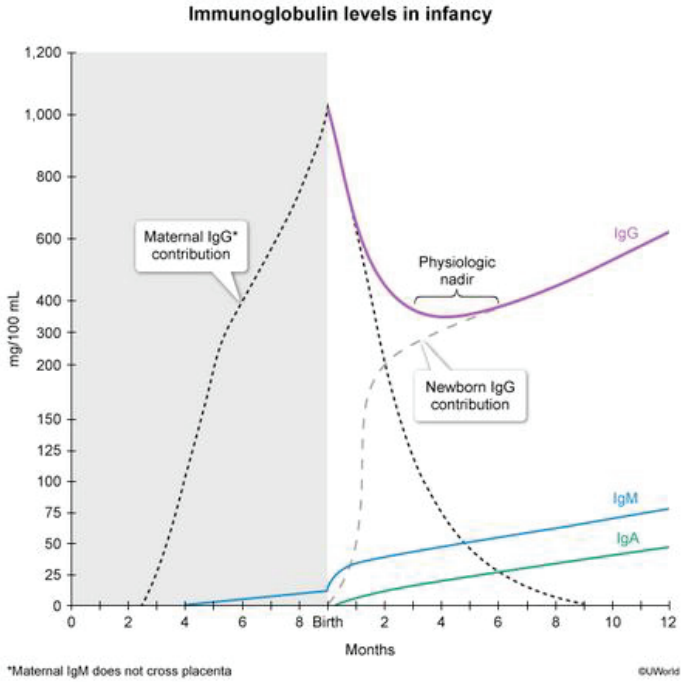
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Growth restriction, microcephaly, hepatosplenomegaly, and a diffuse dark-blue rash (ie, blueberry muffin rash) are nonspecific features shared by multiple **congenital (TORCH) infections** (eg, cytomegalovirus, toxoplasmosis, rubella). These infections are transmitted transplacentally to the fetus from a mother infected during pregnancy. Although maternal symptoms may be mild (eg, fever, lymphadenopathy), the developing fetus can have significant morbidity, particularly with a first trimester infection.

Serology and polymerase chain reaction testing can help to determine the diagnosis in a neonate with suspected intrauterine infection. Neonatal antibody titers can be difficult to interpret, particularly due to maternal transfer of some antibodies and not others:

- Maternal IgM does not cross the placenta, so detection of organism-specific **IgM** in a **symptomatic neonate** is **diagnostic**.
- At birth, virtually all infant IgG is maternally derived IgG that crossed the placenta, and **elevated maternal IgG** would be expected in this mother with infectious symptoms 6-7 months prior to delivery **(Choices A and D)**. Therefore, organism-specific **newborn IgG** (eg, *Toxoplasma* IgG) will also be **elevated** in the setting of a past maternal infection.

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(Choices A and D). Therefore, organism-specific **newborn IgG** (eg, *Toxoplasma* IgG) will also be **elevated** in the setting of a past maternal infection.

(Choice C) Maternal IgM may be negative with a remote infection (as with this mother) or positive if recently infected. False negative IgM titers can also occur in neonates with congenital infection whose IgM waned before birth or in those who have yet to form a robust immune response. However, a positive newborn IgG would be expected due to transplacental transfer of maternal IgG.

Educational objective:

Organism-specific IgM is diagnostic of congenital infection in a symptomatic neonate (eg, growth restriction, microcephaly, hepatosplenomegaly, blueberry muffin rash). Because maternal IgG titers are expected with a past infection and neonatal IgG at birth is maternally derived, elevated newborn IgG is also expected.

References

- Laboratory diagnosis of congenital toxoplasmosis.

Immunology	Infectious Diseases	Torch infections
Subject	System	Topic

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www.ncbi.nlm.nih.gov/pubmed/27147724